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DEPARTMENTS

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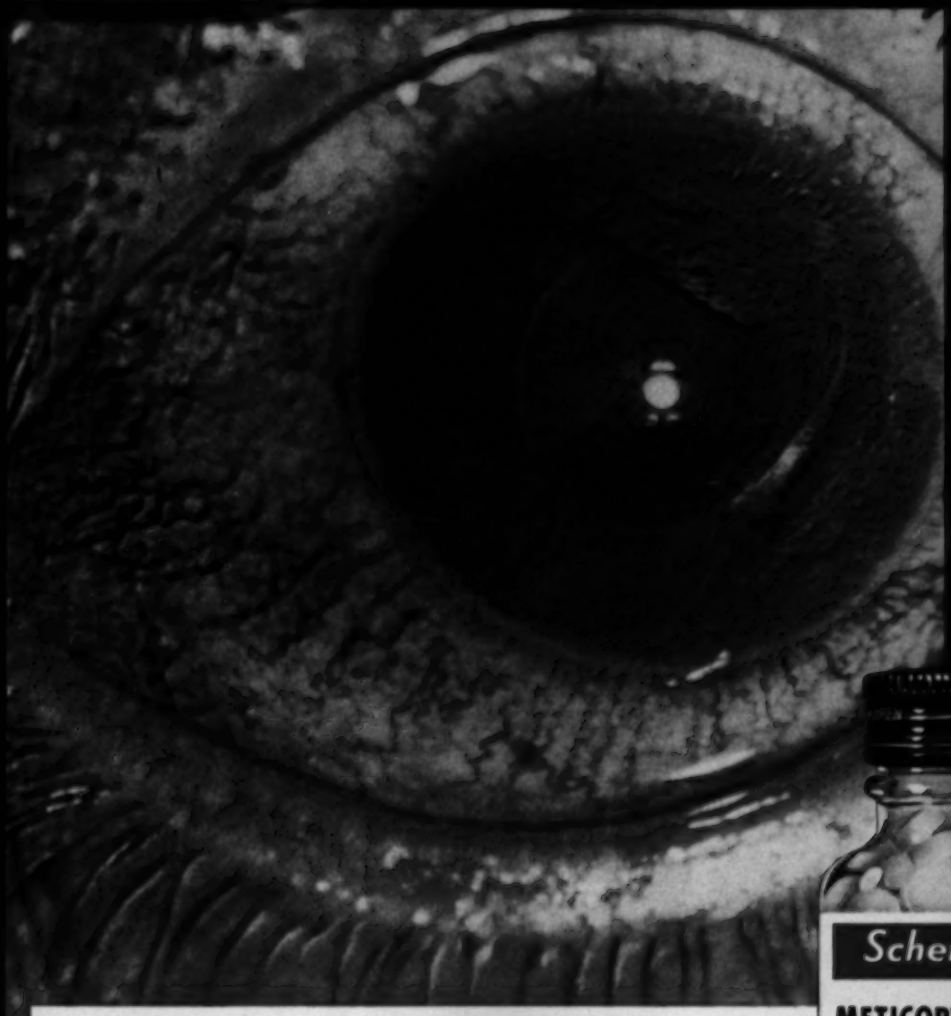

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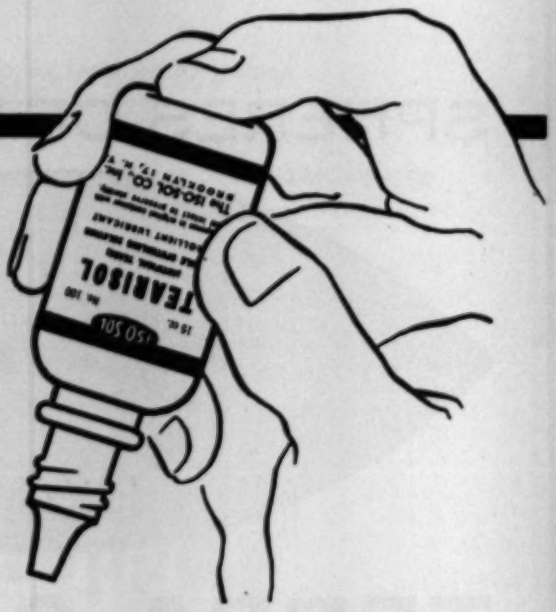

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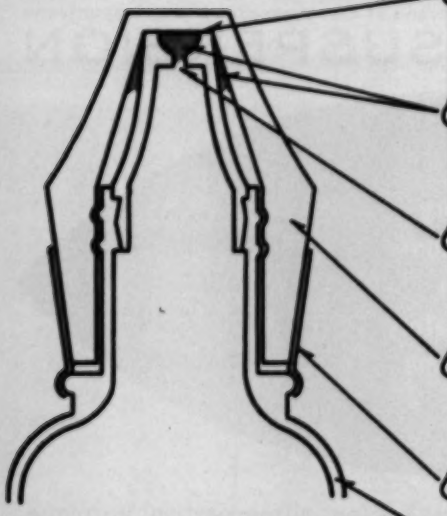

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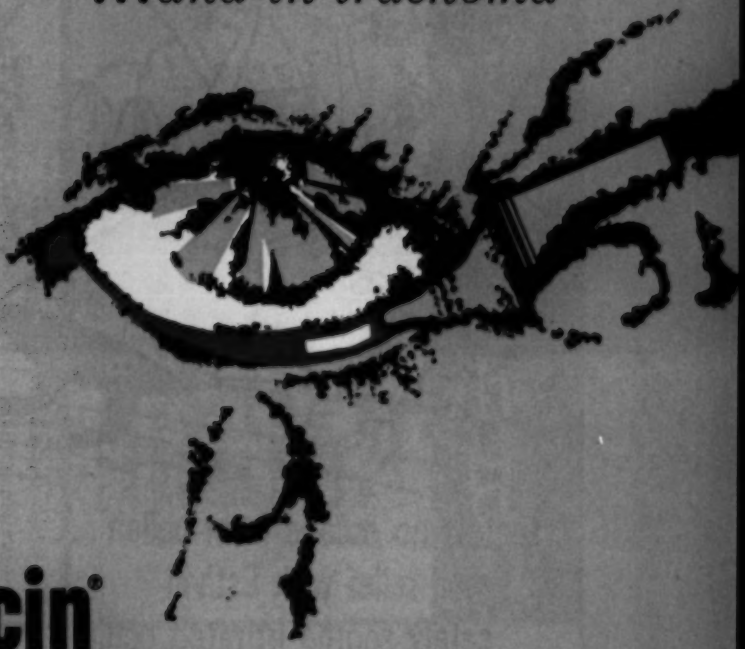

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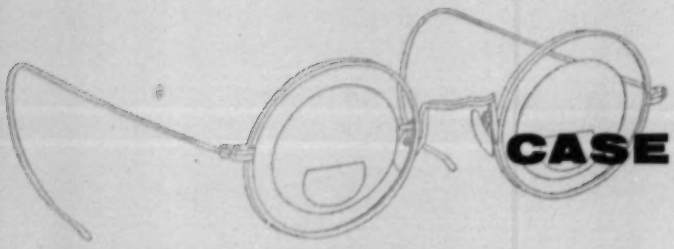

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CASE HISTORY – Mr. F. S.

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3-18-55: Manifest O.D. +10.50Dsph ○ +0.50Dcyl. ax 165 = 20/20–; +2.75D add = Jg. 0.75 @ 12½". Rx Right: Manifest findings in CATAREX T (temporary style) straight-top bifocal. Left: lens to balance.

4-12-55: Right vision with above CATAREX T lens = 20/40+. Manifest O.D. +10.50Dsph. ○ +1.50Dcyl. ax 105 = 20/15+; +2.75D add = Jg. 0.75 @ 13". Patient was allowed to retain first CATAREX T lens until second pair was received with new Rx.

5-5-55: Right vision with 4-12-55 Rx = 20/20. Manifest O.D. +10.000sph. ○ +1.50Dcyl. ax 105 = 20/15+. Again, patient was allowed to retain former lens until the new Rx in CATAREX T was ready.

5-31-55: Right vision with 5-5-55 Rx = 20/50. Manifest O.D. +10.00Dsph. ○ +1.00Dcyl. ax 60 = 20/15+. Rx Right: Manifest findings in CATAREX T. Left: lens to balance.

7-6-55: Right vision with 5-31-55 Rx = 20/20+. Manifest O.D. +10.00Dsph. ○ +1.00Dcyl. ax 75 = 20/15+. Rx Right: Manifest findings in CATAREX T. Left: lens to balance.

7-27-55: Manifest O.D. +10.50Dsph. ○ +1.25Dcyl. ax 90 = 20/15+; +2.75D add = Jg. 0.75 @ 13¾". Rx Right: CATAREX D (permanent). Left: lens to balance.

1-18-56: With permanent CATAREX D lens, right vision = 20/15+; Jg. 0.75 at 13".

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AMERICAN JOURNAL OF OPHTHALMOLOGY

VOLUME 42 JULY, 1956 NUMBER 1

TELANGIECTASIS OF THE RETINA AND COATS' DISEASE*

THE ELEVENTH SANFORD R. GIFFORD LECTURE

ALGERNON B. REESE, M.D.
New York

I can think of nothing that would give me greater happiness than this opportunity to participate in ceremonies commemorating the memory of Sanford Gifford. One can think only of good things to say about him. In one respect, though, I might disparage him. As I look back, I think he was responsible for my starting on a book I wrote called *Tumors of the Eye*. He invited me to address the Chicago Ophthalmological Society and asked me to speak on pigmented tumors of the eye because he said the subject was so confused in his mind. After I had finished my address, he commented in his kind and indulgent way that for the first time he had a clear idea of the subject. I demurred because I knew it was far from clear in my own mind. As a result of this encouragement, however, I distinctly remember amusing myself on the train back from Chicago by projecting an outline to cover other groups of ocular tumors, and this materialized into the book. I hope Sandy will not be held accountable for this in Heaven.

In this lecture I wish to support the thesis that so-called Coats' disease is basically a more or less masked telangiectasis of the retinal vessels. Actually, my purpose is really to integrate two lesions which separately have been appreciated but not in general their relationship. The one is the lesion described by Leber as "multiple retinal aneurysms associated with retinal degeneration" and the other is the dark, globular detachment of the retina usually referred to as Coats' disease. I should like to present the evidence I have accumulated that the two conditions are one and the same, and that essentially Coats' disease is a telangiectasis of the retina.

COATS' DISEASE

Since 1908[1] when Coats gave his excellent clinicopathologic description of a lesion, which subsequently has been called by his name, there has been a broad interpretation of the nature of this lesion. Even to this day the term "Coats' disease" is still ambiguous. There are some who apply it to almost any unexplained acquired tissue in a child's eye. There are others who give it a specific interpretation (Junius,[2] Elwyn[3]).

There are still others who believe that it should not be viewed as a clinical entity but should embrace a number of conditions characterized by massive exudation between the retina and the choroid. In this category Duke-Elder[4] includes (1) external hemorrhagic retinitis (of Coats); (2) external exudative retinitis (of Coats), serofibrinous degenerative retinitis (of Leber); (3) angiomatosis retinae (von Hippel and Lindau—massive exudation with arteriovenous communication of Coats); (4) retinal degeneration with multiple miliary aneurysms (of Leber); (5) disturbances in

* From the Institute of Ophthalmology of the Presbyterian Hospital, New York. Presented before the Chicago Ophthalmological Society, February, 1955. This work has been supported by a grant from the Dunlevy Milbank Foundation, Inc.

the choroidal circulation—the majority may be termed senile exudative choroiditis (senile form of Coats' disease); and (6) traumatic cases from hemorrhage at birth. He felt that clinically the hemorrhagic variety was indistinguishable from the inflammatory.

At the time of his original description in 1908, Coats felt that primarily there was hemorrhage from the capillaries of the outer plexiform layer of the retina and he suggested that the cause of the hemorrhage consisted of a constitutional change in the blood vessels perhaps associated with alteration of the blood. In a later report (1912[5]), he still felt that the primary feature of the disease was hemorrhage in the outer layers of the retina and hence into the subretinal space but he recognized the exudative and inflammatory feature and then suggested the term "external exudative retinitis" instead of "external hemorrhagic retinitis." Three years later, in 1915,[6] Leber suggested that the hemorrhage was incidental and secondary. This view has been later supported by von Hippel[7] and in part by Duke-Elder.[4]

The dark, globular retinal detachment usually referred to as Coats' disease (fig. 1A; fig. 10B) is generally detected for the first time when the completely detached retina, or the reflected light from it, is seen in the pupillary area. The dark and sometimes greenish-brown color is due to hemorrhage and secondary changes. The globular shape is due to the fact that hemorrhage accumulates in the outer layers of the retina or in the subretinal space. The hemorrhage characteristically does not gain access to the vitreous which is relatively clear. Over the area of globular detachment, vascular lesions can seldom be appreciated but occasionally the retina is still undetached, or shows only a flat detachment in a quadrant and here, frequently, an angiomatous process is discernible over the retinal surface (fig. 1B; fig. 9B). Such a process seems to be masked in the opaque detached retina.

Telangiectasis of the retina

The characteristic fundus lesion is a circumscribed, slightly elevated area over which are numerous small, sharply outlined, red globules (figs. 2, 3, 4, 5, 6, 7, 9A, and 10A). At first glance they may resemble retinal hemorrhages or aneurysmal dilatations. Within the lesion area there may be light-colored, opaque regions partly obscuring the angiomatous element. Usually, only one focus is present in the fundus. Very rarely the foci may be multiple with normal-appearing intervening retinal tissue. The lesion is usually unilateral but may involve both eyes (fig. 4). The disc, instead of the retina, may be the site of primary involvement (fig. 7). Apparently as the result of a circulatory disturbance wide areas of the retina may

---

Fig. 1 (Reese). *Coats' disease.*

(A) P. M., a boy, aged five years. There is a dark, bluish, bullous detachment of the retina in which are visible red globules representing telangiectasis.

(B) G.S., a boy, aged five years. There is a dark bullous detachment of the retina. In the upper outer quadrant, the retina is relatively flat and over this area telangiectasis of the retinal vessels can be seen. (Patient of Dr. R. Townley Paton.)

Fig. 2 (Reese). *Retinal telangiectasis.*

A. H., a woman, aged 29 years. The fundus lesion of the right eye was found in a routine eye examination. Vision in this eye was 20/15. No field defect detected on tangent screen. No progression of lesion over a period of six years.

Fig. 3 (Reese). *Retinal telangiectasis.*

S. N., a man, aged 44 years. Fundus picture seen in routine eye examination. No change in 15 years. (Patient of Dr. Kaufman Schlivek and Dr. John H. Dunnington.)

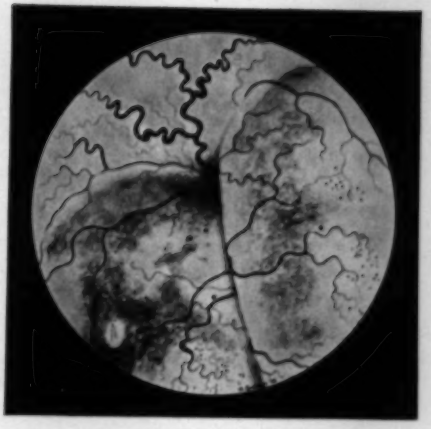


Fig. 1A

Fig. 1B

Fig. 2

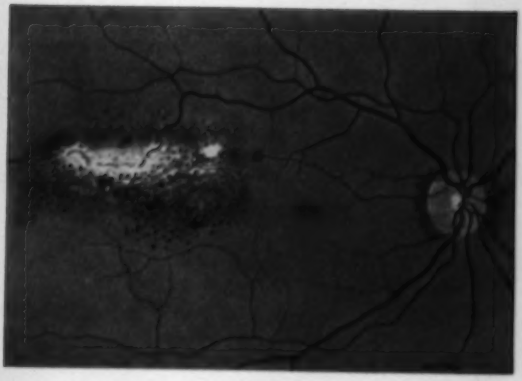
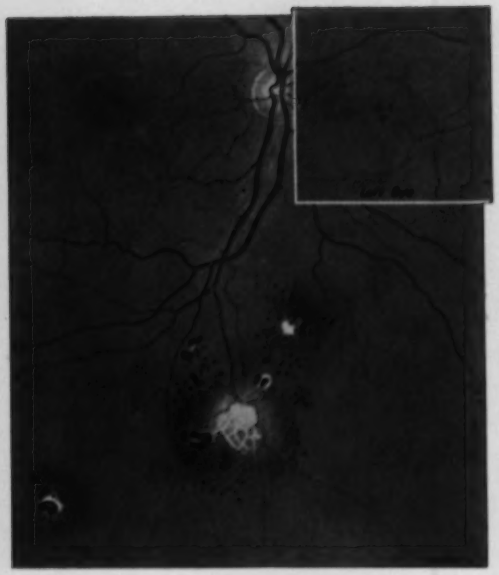


Fig. 3



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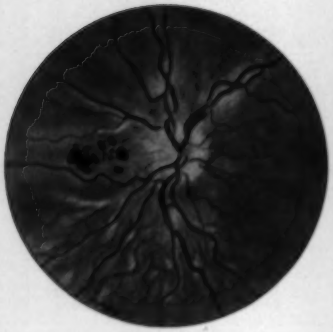

Fig. 6

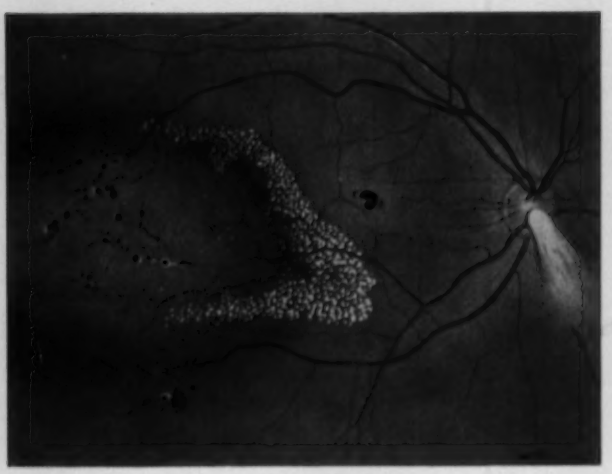

Fig. 5

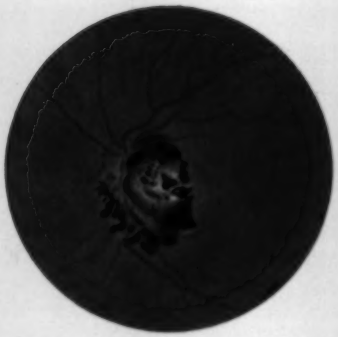

Fig. 7

become whitish in color from stasis or residual edema (fig. 10A). This feature may clear over extensive areas giving the appearance of remission of the process. In the macular area the edema may produce a star (fig. 9A).

The lesion described above may remain essentially stationary, may show inconsequential hemorrhages from time to time, or manifest a progressive course leading to complete detachment of the retina and sometimes to glaucoma and enucleation. It appears to me that the lesion first described by Leber,[8] and subsequently by others, as multiple retinal aneurysms is the same process referred to here.

The disease can hardly be confused with angiomatosis retinae (von Hippel's disease[9]) which is characterized by one or more tumor masses to and from which course a nondescript afferent and efferent vessel. The advanced stage of the two diseases may resemble each other but the age groups characteristically are different.

We know that microaneurysms may occur not only in diabetes but as a result of many other pathologic processes, and particularly as a response to venous occlusion.[10] When the aneurysms occur as a conglomerate mass, they may simulate, clinically, telangiectasis. Such a possible case is shown in Figure 11.

At first, what is now referred to as telangiectasis was called by me capillary hemangioma of the retina and as such several of the cases reported in this paper are described in my book, *Tumors of the Eye*. In this present study I have concluded that the lesion is actually a telangiectasis and confirming this concept is a reconstruction of the vascular pattern as shown in Figure 8. Here we see simple vascular channels the lumina of which vary considerably in size.

A conspicuous feature brought out by the periodic-acid stain is a thick homogeneous basement membrane under the endothelium (figs. 8B, 9C, and 9D). This specifically stained homogeneous polysaccharide is laid down to varying degrees reaching in places a point where the entire lumen appears occluded by it. It is thought, therefore, that the basic change in this disease is the formation of this polysaccharide under the endothelium

Fig. 4 (Reese). *Retinal telangiectasis.*

A. B., a woman, aged 24 years. There is telangiectasis in the right retina, as noted in January, 1949. The insert shows a similar small focus in the left retina. No progression in three years. (Same as Case 2, page 375, *Tumors of the Eye.*) (Patient of Dr. Maxwell A. Mintz.)

Fig. 5 (Reese). *Retinal telangiectasis.*

G. B., a boy, aged 12 years. In the periphery of the fundus temporally there are red globules representing telangiectasis. Central to this is an area of hard, white deposits (residual edema). Some white sheathing of veins. Anterior to the disc there is some white opaque tissue and from this some remains of the hyaloid artery extend through the central part of the vitreous and in part even to the posterior surface of the lens. No change in the condition in eight years.

Fig. 6 (Reese). *Retinal telangiectasis.*

R. B., a boy, aged 15 years. The fundus picture shown here was detected in a routine eye examination because of headaches. The fields on the tangent screen were normal. Neurologic examination—including X-ray studies, electroencephalogram, and pneumoencephalogram—was negative. X-ray films of the optic foramen were negative. There has been no progression of the fundus lesion in two years.

Fig. 7 (Reese). *Telangiectasis over the disc.*

J. E., a boy, aged 14 years. Fundus changes were noted in routine examination. Vision, O.U., 20/20. Subsequently there have been several episodes of hemorrhage from the lesion into the vitreous. These have always cleared and left normal vision. Over a period of 20 years there has been a slight increase in the size of the lesion which covers the lower half of the disc and projects into the vitreous from four to six diopters. (Patient of Dr. John H. Dunnington.)

leading to atresia and even occlusion of vessel lumina and thereby occasioning vascular ectasia and the formation of collateral channels.

The passive congestion from atresia and occluded vessels leads to edema which explains the changing fundus picture and the hemorrhage. The latter is characterized by extending externally toward the subretinal space leading in progressive cases to detachment of the retina (Coats' disease).

Cases which have been followed through the transition from a telangiectasis of the retina to a dark, globular detachment of the retina (Coats' disease)

We have been able to follow two patients with telangiectasis of the retina through the metamorphosis to Coats' disease with subsequent pathologic examination of each eye (figs. 9 and 10). This has been possible through the courtesy of Dr. Arthur Unsworth in one case and Dr. Abraham L. Kornzweig in the other. Both eyes were ultimately enucleated because of secondary glaucoma.

The microscopic examination of these two eyes (figs. 9C and 9D) showed acquired vascular channels in the inner layers of the retina. These vessels are brought out particularly well with the periodic-acid stain (Hotchkiss[11]), which stains brilliantly red the basement membrane of the endothelium. The technique is a great help in the study of these eyes for with the usual stains the vascular character is much more subtle (fig. 9E). The channels vary considerably in size from congeries of capillaries to cavernous spaces and show variations in the caliber of their lumina amounting to aneurysmal dilatations in places. The walls and lumina of the newly formed channels show a homogeneous red-staining material similar in character and continuous with the basement membrane. In places the channels appear completely occluded by this material.

Hemorrhage occurs from the blood sinuses and courses through the external layers of the retina to the subretinal space. The hemorrhage becomes organized or undergoes changes to hemosiderin and crystals. Sometimes large blood cysts are formed protruding from the external surface. In these cysts are hematogeneous debris and giant cells. Such a large cyst

---

Fig. 8 (Reese). *Reconstruction of the pattern of the telangiectasis in the retina which leads to Coats' disease.*

(A) The model, reconstructed from sections of the above eye by Mr. Edward Gonzalez, M.T. (ASCP), shows a congeries of vascular channels with various degrees of dilatation. Those stained red are open channels and those stained blue are occluded partially or totally by a homogeneous substance identified specifically by the periodic-acid stain as a polysaccharide.

The plan of reconstruction was the following:

The globe was embedded in celloidin and by the dry method 10 mμ serial sections were cut. Every 10th section was projected on a screen and the vascular channels magnified ×100 were traced on paper. Each vessel lumen was cut out and a replica was made in polyethylene which was one-mm. thick. These replicas were superimposed sequentially thus giving the reconstructed channels as shown in the illustrated model. The replicas of the channels which were patent were stained red with eosin and those which were partially or totally occluded were stained with hematoxylin.

From these reconstructed vessels it seems apparent that the vascular lesion here is a telangiectasis. It is postulated that the cause is due to atresia produced by the formation of the subendothelial material.

(B) A section of the retina from the left eye of a boy (S. McB.) aged three months. The clinical picture was said to be consistent with Coats' disease. Tufts of newly formed, dilated blood vessels were described over the retinal surface. There was some buphthalmos and the intraocular pressure was 46 mm. Hg (Schiøtz). After microscopic examination the diagnosis was Coats' disease. The periodic-acid stained sections show retinal vessels with varying sized lumina all of which have a thick, red-staining, subendothelial layer. Depending upon the amount of this homogeneous material there exist degrees of vessel atresia and some vessels seem to have their lumina completely occluded. These vessels have been reconstructed and the model is shown in (B).

Fig. 8A

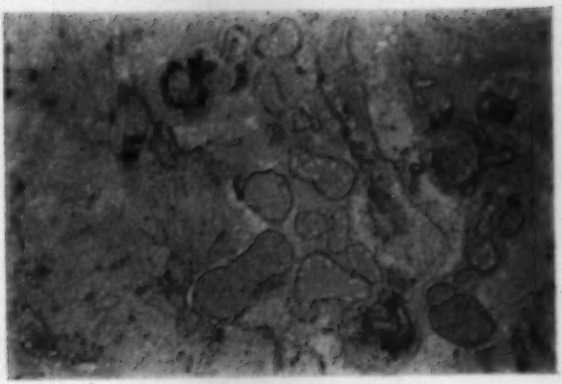

Fig. 8B

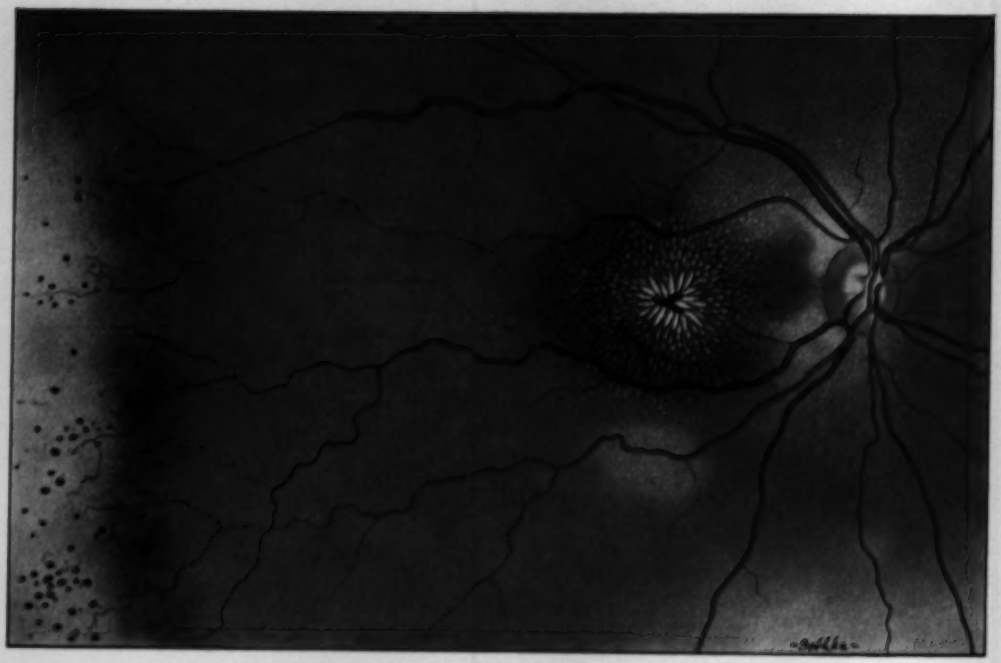

Fig. 9A

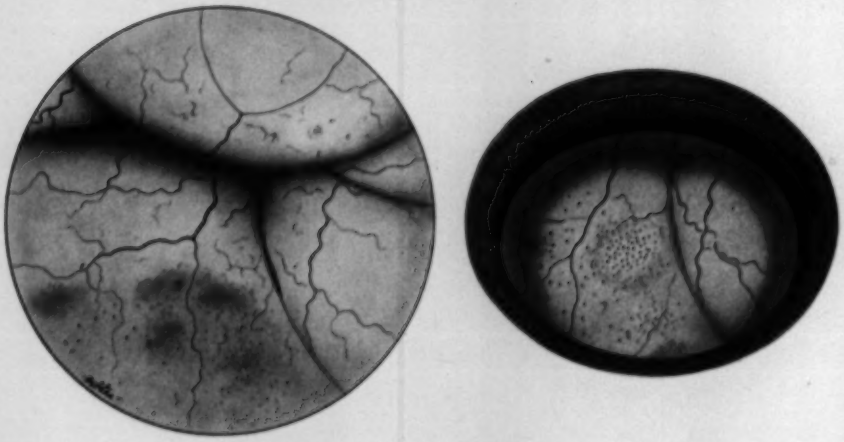

Fig. 9B

may press against the choroidal surface and produce proliferative changes in the pigment epithelium. The metaplastic fibrous tissue thus formed may adhere the retina to the choroid, especially in the macular region, or, the retina may eventually detach itself leaving the proliferative changes partly over the choroidal surface and partly in the retina.

A conspicuous feature in the retina is hyaloid eosin-staining foci representing residual edema. This tends to accumulate particularly in the external plexiform layer. This inspissated edema, along with an apparent increase in the glial or fibrous element which tends to replace the nuclear layers, accounts for some of the increased thickness of the retina.

There is some tendency to perivascular infiltration of lymphocytes but whether or not this is due to an actual inflammation which is a part of the process or due to the toxic effects of the old hemorrhage cannot be said.

In our collection I have reviewed the sections of globes enucleated with the clinical diagnosis of Coats' disease or pseudoretinoblastoma and I find 10 that show angiomatous changes in the retina similar to those seen in the two above-mentioned cases and in Figure 8B.

Discussion

I think the vascular lesion in the retina in these cases should be viewed as a telangiectasis rather than as a hemangioma. This is based on the fact that the abnormal vascular channels are dispersed throughout the retina having retinal tissue as their stroma instead of a stroma of their own. The lesion is not essentially that of aneurysms. Aneurysmal dilatations do occur but of acquired channels and not of the pre-existing ones. The lesion seems to be on the venous rather than the arterial side of the vascular tree.

The fundus lesion of one patient followed now for over eight years was thought at first to be telangiectasis of the retina (fig. 11) and therefore to belong to the group described here. The subsequent course, though, indicates clearly that, although the fundus picture simulates this group, actually the lesion is basically different. It probably should be grouped as an Eales' disease with the understanding that this term probably embraces a heterogeneous group.

The areas of dilated telangiectaticlike vessels may be the result of anoxia from vascular occlusion.[10] This case has been included in the report for it represents a condition which clinically can simulate the lesion under discussion and therefore may come up for differential diagnosis.

There is some evidence that this telangiectasis of the retina described here has a relationship to Osler's disease or hereditary hemorrhagic telangiectasis. Oravisto's case[12] had epistaxis and telangiectasis of the face and cuticle; Mylius' case[13] had telangiectasis of the breast and nail bed; Junius[14] thought that there may be telangiectasic lesions anywhere over the body and Spadavecchia's case[15] was associated with telangiectasis of the skin. One of our cases[16] had telangiectasis of the skin of the upper lid on the affected side. Another had localized telangiectatic vessels of the conjunctiva of the affected eye. We have noted no hereditary aspect to our cases.

Reports in the literature supporting the

Fig. 9 (Reese). *Retinal telangiectasis which progressed to Coats' disease.*

R. M., a girl, aged 13 years, noted increasingly blurred vision of the right eye for three months.

(A) Appearance of right fundus, May, 1949. The telangiectatic blood vessels are seen temporally in the white opaque retina. There is a white star of the macula.

(B) Appearance of right fundus, June, 1950. The telangiectatic blood vessels and some hemorrhage are seen over the dark bullous detachment (Coats' disease).

thesis that Coats' disease stems from an angiomatous process of the retina are the following:

1. The clinical appearance documented with the microscopic findings by Klien,[17] Miyashita and Nisyake,[18] Mylius,[13] and Gourfein-Welt.[19]

Klien gives an excellent fundus drawing showing the typical picture and microscopic sections of the eye with changes identical to those in the eyes I examined. Miyashita and Nisyake's case supports this thesis. They assume that the basic process is inflammatory with maybe hereditary weakness of the vessel walls. Degeneration of the vessel walls takes place with dilatation and convolutions leading to thrombi.

Mylius associated aneurysms of the retinal vessels with Coats' disease. Gourfein-Welt related Coats' disease to a vascular lesion of the retina. In this case there was a typical advanced Coats' disease in one eye which was enucleated and a small area of vascular disease simulating the type described here in the fellow eye.

2. The microscopic findings by Givner.[20] He depicts microscopic sections with typical change and expresses views similar to those in this paper.

3. The clinical appearance by Fisher,[21] Pringle,[22] and Guzmann.[23] Fisher and Pringle called the fundus lesions aneurysms of the retinal vessels.

I believe that the term "Coats' disease" should be restricted exclusively to the characteristic and rather constant clinical picture of the dark, and maybe greenish colored, bullous detachment of the retina of young children, the angiomatous nature of which can often be appreciated at some site where the retina is still more or less in situ, particularly if an adequate examination is done under general anesthesia. When a telangiectasis of the retina is seen, it should be viewed as a precursor of Coats' disease but not in an obligatory sense. Such retinal telangiectasis may remain static, may progress to complete detachment of the retina (Coats' disease), or may give rise to hemorrhages from time to time with no serious secondary changes.

Progressive fundus changes may occur followed by marked spontaneous regression. This seems to be due to residual edema which may absorb. The edema causes a silver-white appearance of the fundus (fig. 10A) which may affect a part or all of the fundus. I have noted this progressive change followed by regression in two of my cases. A striking instance of this is a case reported in 1914 by Friedenwald.[24] The lesion had progressed to a point where the retina in the macular region was elevated eight diopters. A later report on this patient in 1929[25] indicated that regression had occurred so that the fundus changes consisted merely of pigment disturbances, particularly around the macular region. In a personal communication, I understand that few additional changes have occurred to date, except that, in 1952, there was a sudden rather large vitreous hemorrhage. The hemorrhage absorbed slowly and the appearance of the fundus now is not very different from that seen previously.

The periodic-acid stain brings out the thick homogeneous basement membrane of the vascular channels composing the lesion and also accentuates the occurrence of large masses of similar substance which partially or totally occludes the lumina of the vessels. The affinity of this material for this stain identifies it as a polysaccharide. The basic

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(C) A section of the retina of this eye showing the large blood vessel whose wall is thickened by the red, homogeneous material. Above this vessel is a smaller occluded vessel whose lumen is completely filled with the red substance (periodic-acid stain).

(D) A section of the retina of the same eye showing large vascular channels whose walls are either thickened to various degrees or are occluded by the red homogeneous material (periodic-acid stain).

(E) A section of the same lesion in the retina of this eye stained with the usual hematoxylin and eosin. By contrast it can be seen how specific the periodic-acid stain is.

(Same as Case 3, p. 377, *Tumors of the Eye*. Patient of Dr. Arthur Unsworth.)

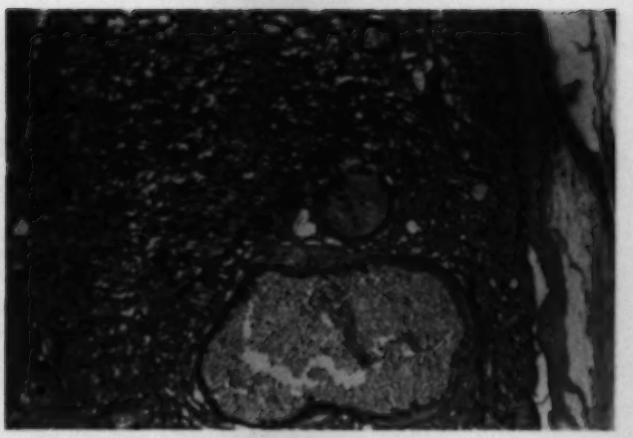

Fig. 9C

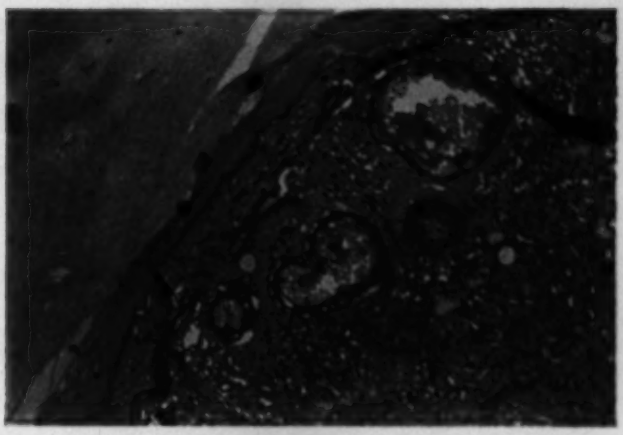

Fig. 9D

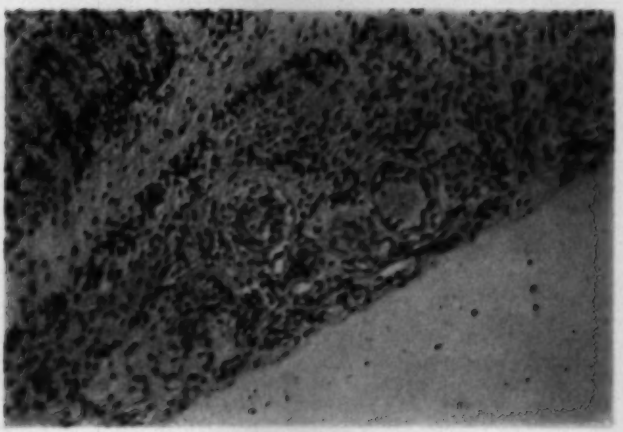

Fig. 9E

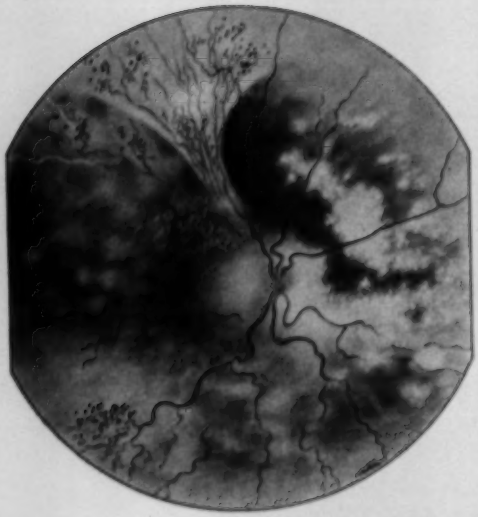

Fig. 10A

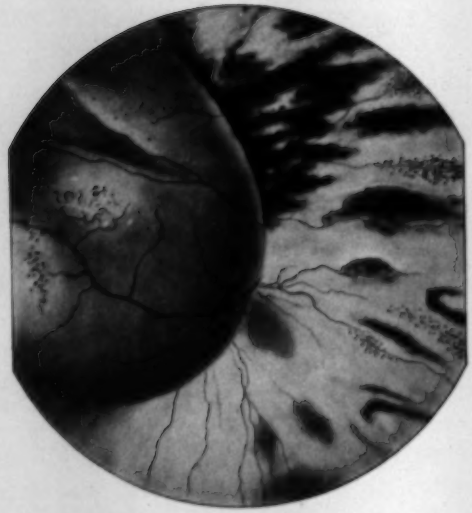

Fig. 10B

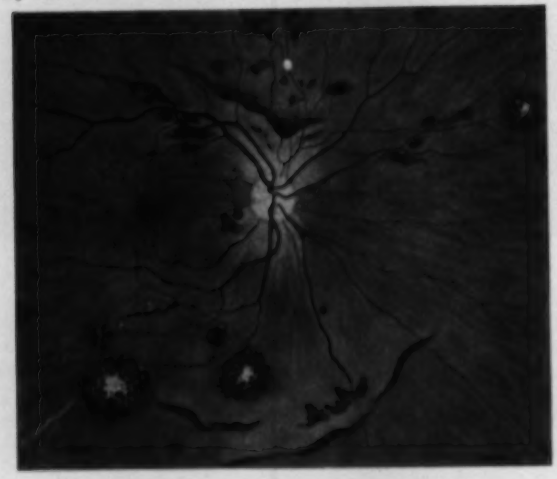

Fig. 11

pathologic process in the occurrence of Coats' disease could, therefore, be the formation of this polysaccharide supposedly by the endothelium of the retinal veins. This causes various degrees of vascular atresia and even complete occlusion which in turn produces vascular ectasia and newly formed collateral vessels. The remissions in the fundus picture mentioned above are probably due to occluded vascular channels which later become compensated for by the development of collateral circulation.

In view of the uncertain course, the question arises as to what, if anything, should be done in the way of therapy should the retinal telangiectasis be noted in the early stages. We have given radiation to two eyes according to the technique we use to treat patients with retinoblastoma. These cases are the following:

1. A rather advanced case, shown in Figure 10 in the legend of which the radiation factors are given. The lesion progressed and the eye was enucleated.

2. An advanced lesion which received X-ray treatments with the following factors: 220 kv.; 0.5 Cu + 1.0 Al filters; 20 ma.; 50 cm. T.S.D.; 3.5 cm. cone to right temporal portal, 250 r − Rx t.i.w. × 4 = 1,000 r. The patient was a female, aged 16 years. There has been regression of the edema as well as of the actual lesion and

←

Fig. 10 (Reese). *Retinal telangiectasis which progressed to Coats' disease.*

G. P., a boy, aged 10 years. For five months the vision in the right eye had become progressively poorer. Examination showed the retina of the right eye to be white from what seemed to be residual edema. In the upper outer quadrant there was an elevated area over the surface of which were many circumscribed red globules interpreted as dilated or ectatic vessels. In the retina elsewhere there were also similar vessels. Also, an area of dilated tortuous vessels was present in the bulbar conjunctiva at the limbus from the 2- to 3-o'clock position.

(A) Appearance of right fundus October, 1953. Telangiectatic vessels are seen and the light color is due to residual edema. There is beginning elevation of the retina in the upper outer quadrant. Radiation was given by the method employed for treating retinoblastoma (Arch. Ophth., **27**:40-72 [Jan.] 1942). The factors were 220 kv.; 20 ma.; 0.5 Cu + 1.0 Al filters; 50 cm. T.S.D.; 2.5 cm. portal, 500 r − Rx b.i.w. × 3 = 1,500 r to right temple.

(B) Appearance of the fundus March, 1954. The detached retina has progressed to a large, dark, bullous mass. The eye was enucleated and sections show a vascular lesion characterizing the group discussed here. (Patient of Dr. Abraham Kornzweig.)

Fig. 11 (Reese). *Eales' disease simulating telangiectasis of the retina.*

D. B., a man, aged 28 years. The patient noted a disturbance of vision in both eyes, particularly the left one, for the past three years. At the onset of symptoms, noted first in the left eye, he was told there was a hemorrhage. Prior to this, over a period of about three years, his eyes were examined in the Navy about six times and no pathologic change was noted.

When seen in February, 1948, the right eye vision was 20/15 and there were, in the lower half of the fundus, two areas of dilated retinal vessels about one disc diameter in size. There were also two smaller but similar areas in the upper half of the fundus. Some of the small arterioles showed sheathing and there was one medium-sized arteriole crossing in the region of the involved areas below which was silver-wire in appearance.

The left eye vision was 20/70 and there was a detachment of the retina below and over the surface many areas of dilated vessels were seen.

In March, 1948, radiation was given with the following factors: 220 kv.; 20 ma.; 50 cm. T.S.D.; 0.5 mm. Cu + 1.0 mm. Al filters; 2.5 cm. portals, 500 r per treatment for a total of 2,500 r × 2—Right temple: 2,500 r and left temple 2,500 r.

The appearance of the lesion in the right fundus in March, 1954, is shown in the drawing. The two foci of dilated vessels are seen below and another above and nasal to the disc. There are some streaks of hemorrhage in the vitreous, and between the retina and the hyaloid membrane, in the lower part of the fundus and just above the disc. The lesions in this eye have shown no progression but actually the foci of vessels seem to be more sclerosed and smaller. The vision is still 20/15.

The process in the left eye progressed to retinitis proleferans, complete detachment of the retina, dense cataract, and secondary glaucoma so that enucleation was necessary.

Sections of the enucleated eye show a generalized sclerosis and marked atresia of the retinal vessels. The periodic-acid stain shows no selectivity. Long strands of fibrous tissue with many blood vessels extend into the vitreous from the detached retina.

now, three and one-half years after the radiation, the lesion seems to be stationary.

I think diathermy applied to the scleral surface corresponding to the site of a localized area in the fundus should be an effective measure.

Conclusion

The term "Coats' disease" is loosely used and often serves as a waste basket for unexplained instances of leukokoria. In this presentation I have attempted to give to the conception of Coats' disease a sharper delineation based on the contributions of others as well as on personal observations. I hope I have been able to throw some light on a subject which has been equivocal since "the memory of man runneth not to the contrary." Forbid that I solve it completely! Think how much diversion we shall miss if we ever do know the answers to our moot questions which afford us so much fun in discussion and make such pleasant gatherings as this possible.

73 East 71st Street (21).

I wish to express my gratitude to Miss Lilly Kneiske for her help, and to Mr. Edward Gonzales for the technical work especially the reconstruction shown in Figure 8. I am again indebted to Mr. Gustav E. Bethke for his unusually good fundus drawings.

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JENSEN'S JUXTAPAPILLARY RETINOPATHY*

(IDIOPATHIC FOCAL RETINAL ARTERIOLITIS)

BERTHA A. KLIEN, M.D.
Chicago, Illinois

In recent years, attention has been focused upon some diseases which are based upon constitutional anomalies. They belong to either one of two groups, each of them characterized by a constitutional common denominator.

In one group, this constitutional factor is an abnormal functional state of the autonomic nervous system, which gives rise, under certain circumstances, to recurrent functional vascular disturbances in the retina or choroid, producing the pictures of central angiospastic retinopathy, chorioretinopathy, or choriopathy.

In the other group, the common denominator is a peculiar response of the connective tissue of the body, or more specifically of the interfibrillary ground substance (collagen) to a variety of heterogeneous stimuli with mucoid degeneration and a variable amount of leukocytic infiltration. Collagen being an integral part of the walls of blood vessels, the vascular component not infrequently dominates the clinical picture in these diseases, including that of the eyegrounds (Klemperer,[1] Polley,[2] Christensen[3]).

The possibility of fundus lesions on the basis of collagen degeneration without demonstrable systemic disease also exists and should be considered among others for Jensen's juxtapapillary retinopathy. As Stillerman[4] stated, the scope of purely or predominantly ocular disease on this basis may be widened as more information on a variety of so far obscure diseases is collected.

Juxtapapillary retinopathy was first described by Jensen[5] in 1903.

The classical ophthalmoscopic picture in the acute stage of the disease consists of retinal edema in one sector of the fundus usually contiguous with the optic disc, and of a group of feathery, white, "cotton wool" patches within the edematous portion (fig. 1). A variable number of small lipoid deposits may appear within this area somewhat later. Occasionally exudates and hemorrhages are scattered over the same area.

In the course of several weeks or months all evidence of the disease may disappear, or residual findings such as a localized narrowing of the retinal arteriole supplying the affected sector of the fundus, or mild pigmentary disturbances, or both, may mark its former site (fig. 2).

The outstanding subjective symptom, in addition to a very variable degree of diminution of the central visual acuity, is a sector-shaped defect of the visual field, which extends from the blindspot to the periphery (fig. 3) and which may be transient or permanent, or partly regressive.

Surveying the literature on Jensen's juxtapapillary "chorioretinitis," it soon becomes obvious that two different conditions are discussed under this term.

In one group of cases there is undoubtedly a primary choroidal lesion, often of the hypertrophic granulomatous type, which leads, by virtue of its location adjacent to the entrance canal of the optic nerve, to damage of some nerve fibers and of the overlying retina. An inevitable subjective manifestation of this juxtapapillary damage to the nerve fibers, which are bunched together in this region, is a sector-shaped defect of the visual field. In a high percentage of the cases of this group the tuberculous nature of the lesion could be demonstrated (Riehm,[6] Schieck,[7] Rönne,[8] Löwenstein,[9] Gilbert,[10] et al.).

* From the University of Chicago Foundation for Ophthalmic Research.

The well-known fact that one site of predilection of solitary tubercles is near the optic disc bears emphasis in respect to the cases of this group. There appears to exist no valid reason for separating these juxtapapillary lesions from similar chorioretinitic foci elsewhere in the fundus. A histopathologic study of such a case was made by Abraham.[11]

The second group of cases is more distinctive and around them the battle for proper terminology has been raging. It was recognized from the beginning that the fluffy white lesions commonly called cotton-wool patches are part of the acute stage. Their characteristic striate pattern and serrated margins created the correct impression that the main pathologic process was located in the inner layers of the retina, particularly in the nerve-fiber layer. At the same time it led to the erroneous assumption that these lesions represented a primary disease of the nerve fibers, namely a neurofibrillitis (Riehm,[6] v. der Hoeve,[12] Pallares,[13] et al.).

One of the most interesting recent publications on this subject is by Diener[22] who likens the disease to a simple optic neurits. He points out that the nerve fibers in the retina and optic nerve are a functional unit representing the third retinal neuron. He considers the "retinitis juxtapapillaris" a special form of neuritis similar to the neuritis axialis chronica of viral origin of the encephalitic type. This process would be not so much an inflammation as a primary degeneration. He suggests that toxic amblyopias and many cases of retrobulbar neuritis may belong to the same group of diseases. Diener feels that Zeeman's[24] term of "retinal neuritis" is the most suitable for Jensen's juxtapapillary disease.

With the new knowledge gained a few years ago through the demonstration by Friedenwald[14] of the basic pathology of cotton-wool patches as ischemic infarcts in the retina resulting from occlusive arteriolar disease, a re-evaluation of certain fundus pictures should have been started immediately. Jensen's juxtapapillary retinopathy is only one of them.

A localized disease process in one of the larger arterioles near or on the disc with marked narrowing of its lumen and spastic or thrombotic occlusion of some of its terminal branches would explain all objective and subjective findings characteristic of this disease, namely segmental retinal edema, cotton-wool patches, occasional hemorrhages and exudates, and the sector-shaped defect in the visual field.

The occlusive disease could conceivably be all spastic, but the clinical picture, especially of the residual findings, suggests the presence of at least one inflammatory focus centering around an arteriole, such as might develop secondary to fibrinoid degeneration of its wall. Reactive spastic contractions in the pertinent precapillary and capillary beds could give rise to multiple ischemic infarcts (cotton-wool patches).

The retinal instead of the choroidal site, and the vascular nature of the pathologic process in Jensen's disease, is suggested also by occasional white sheathing or small white nodular swellings in the course of some arteriolar branches, which were observed by some in the affected area during the acute stage (Verhage,[15] Riehm,[6] Blessig,[16] Fuchs[18]).

Residual localized arteriolar constrictions at the former site of the lesions reported by others are of similar significance (Cowan,[17] Riehm,[6] Blessig[16]).

The paucity of residual findings otherwise bears emphasis (Groes-Peterson[19]). There may remain slight pigmentary disturbances at one or more places within the formerly involved sector (fig. 2) which should not be interpreted as choroidal damage or as suggestive of a primary choroidal lesion. Voluminous intraretinal edema may destroy some retinal elements and may in this way reach the subretinal space through openings in the external limiting membrane and cause

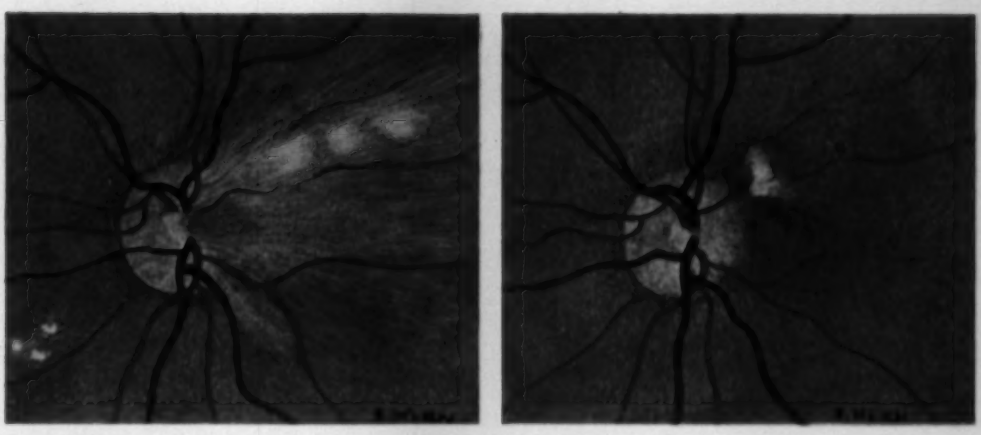

Fig. 1 (Klien). Jensen's juxtapapillary retinopathy. R. E., female, aged 15 years. Vision: R.E., 1.5-2. Severe hay fever. Blurring of inferior temporal field noted for two weeks. Findings are (1) nasal half of optic disc and adjacent retina edematous; (2) three fluffy, cotton-wool patches along a superior nasal arterial branch, which is partly buried in edema; (3) small group of lipoid deposits temporal to disc. Period of observation six years; no increase in central vision.

Fig. 2 (Klien). Right fundus of same patient as in Figure 1 after four years, showing (1) circumscribed attenuation of superior nasal arterial branch, formerly accompanied by ischemic infarcts; (2) one area of white fibrous tissue and two areas of pigment proliferation within area of former retinal edema.

Fig. 5 (Klien). Arterial disease of retina, possibly of similar nature as that leading to Jensen's juxtapapillary retinopathy. A man, aged 55 years. Blurring in left lower visual field noted for 10 days. Vision: L.E., 1.5. Findings are (1) edema of upper pole of disc and adjacent retina, large flat hemorrhage and two "cotton-wool" patches along superior temporal artery; (2) yellowish white sheathing of superior retinal artery after its division into three branches. Period of observation seven years: no decrease in central vision.

irritative proliferation of the pigment epithelum. The resulting subretinal mounds may retain their pigment content and remain visible later as scattered brown patches or they may gradually lose their pigment and become clinically invisible or, depending on their size, remain faintly visible as yellowish flecks. The intensity of the pathologic process is obviously quite variable and upon it would depend the extent of destruction of the retinal elements and the final presence or absence of residual pigmentation.

The etiology of the segmental vascular disease which produces the picture of Jensen's retinopathy appears to be quite varied. Allergic states are found in many of these patients. Sensitivity to tuberculin has been reported in many instances (Riehm,[6] Posthumus[23]). Syphilitic infection was found by Fuchs,[15] Pavia,[20] Verhoeff,[21] and Zeeman.[24]

In this connection the association of Jensen's retinopathy with ophthalmic migraine is interesting (Blessig,[16] et al.). In many patients, however, if at all, allergic states of the more common variety, such as hay fever or food allergies, are the only demonstrable systemic disorders.

Regarding the constitutional factor, it is

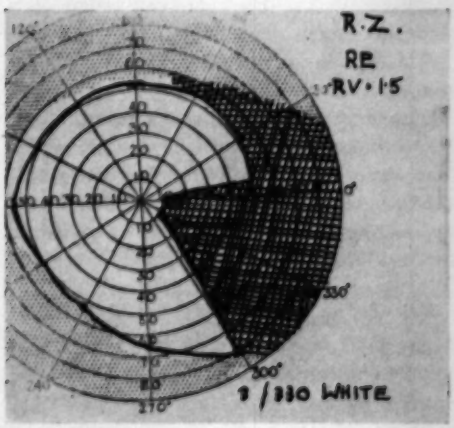

Fig. 3 (Klien). Visual field of right eye of same patient as Figure 1. Sector-shaped defect extending from blindspot to periphery.

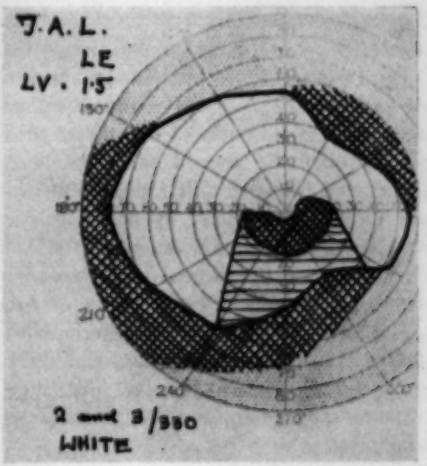

Fig. 4 (Klien). Visual field of left eye of same patient as Figure 5. Pericentral scotoma below fixation point and dent in periphery connected by a zone of relative scotoma.

perhaps of significance that clinical and experimental evidence has been accumulating which points to the intimate relationship between the collagen disorders and immune processes (Fischel,[25] Kampmeyer,[26] and Rich[27]). Hypersensitivity and allergy, especially of the humoral type, have long been associated with some of the diseases now included in this group.

It is conceivable that a purely ocular manifestation, such as the segmental arteriolitis in Jensen's disease, may point to the presence of a constitutional factor similar to that found in a more obvious collagen disorder. It would be interesting to determine by long range observation the cause of the eventual death of patients, who once had an idiopathic focal retinal arteriolitis such as seems to underlie Jensen's disease.

It bears emphasis that the cotton-wool patch is the pathologic finding which frequently dominates the fundus picture in collagen disorders, just as it is the most characteristic lesion in the acute stage of Jensen's disease, and the one whose specific and characteristic appearance led to so much

speculation about the true nature of this disease.

The concept of the intimate relationship between allergy and hypersensitivity, and the tendency to fibrinoid degeneration of the interfibrillary ground substance in response to a variety of noxious agents, has only recently been based upon a more solid foundation through the study of the anti-allergic therapeutic effects of the steroid hormones.

The practical value of the differential diagnosis between true Jensen's disease and a juxtapapillary solitary choroidal tubercle lies in the therapeutic application of these newer principles.

Report of cases

Case 1

R. Z., a girl, aged 16 years, stated that seven weeks prior to her first visit to the office (June) she had experienced a period of blurred right vision, lasting about 10 days.

From April to September every year she had suffered from severe hay fever, which was brought somewhat under control during the past few years by desensitization. Occasionally she had an attack of asthma when around cats.

The tuberculin test was slightly positive (1:10,000) but chest films were always negative. All other physical findings and laboratory tests were normal.

At the time of the first visit her corrected right vision (-3.25 D.sph. $\bigcirc$ -0.5D. cyl. ax. 90°) was 1.5 − 2 and J1, the left vision (-3.0D. sph.) was 1.5 and J1.

In the right visual field there was a sector-shaped defect which radiated from the enlarged blindspot to the inferior temporal periphery (fig. 3) being separated by 10 degrees from the fixation point.

The right fundus (fig. 1) showed the classical picture of Jensen's juxtapapillary retinopathy. There was a sector-shaped area of retinal edema which extended mainly nasally and upward but involved also the center and upper half of the optic disc. Two retinal arterioles were running peripheralward within this edematous area, being buried in several places within the edema, so that it was uncertain whether or not they were actually narrowed at any place. Between these two arterioles there was a chain of three cotton-wool areas. Inferior and temporally to the disc there was a group of small lipoid deposits. They suggest that the edema of the optic nerve might have been more extensive at the time of the visual disturbance seven weeks prior to the time when this picture was made.

The left eye was normal in every respect.

During the next few months of observation several small hemorrhages appeared below the most proximal cotton-wool area. Within a year the edema of the optic nerve had completely disappeared and the retinal edema had become rather circumscribed in the region of the former cotton-wool areas.

After four years (fig. 2) a small patch of fibrous tissue was overlying the larger (more inferior) of the two arterioles mentioned before. Peripheral to this patch the arteriole showed a focal narrowing. There were also several faintly pigmented areas scattered within the formerly edematous segment.

This fundus picture has not changed up to the present time.

The visual acuity of this eye has remained 1.5 throughout the period of observation. The sector-shaped defect of the left visual field has remained but has receded to 20 degrees from the point of fixation as compared to the 10 degrees when first charted.

Case 2*

T. A. L., a man, aged 56 years, had a known corrected visual acuity of 1.5 in each

*I am indebted to Dr. W. F. Moncreiff for permission to paint the fundus of this patient and for all other information concerning progress and medical examinations.

eye for seven years prior to the present complaint. For the past 10 days he had noted a blurred area in the left visual field just below the fixation point.

The visual acuity of the left eye was still found to be 1.5, but perimetric examination revealed a large arcuate pericentral scotoma below the fixation area, sparing the point of fixation by two degrees. There was also an indentation of the superior and inferior quadrants of the peripheral field. The inferior peripheral defect was connected with the pericentral scotoma by an area of relative scotoma, adding up to a sector-shaped defect of the visual field (fig. 4).

The superior branches of the left central retinal artery had dull white sheaths on and shortly beyond the disc. Along side the middle branch there were two cotton-wool patches, and further peripherally there was a flat, one disc diameter in size, superficial retinal hemorrhage (fig. 5).

General medical examination was completely negative and the patient was placed on intravenous typhoid vaccine therapy.

The cotton-wool areas and the hemorrhage gradually disappeared during the following six months and the sheaths along the superior arterioles became less opaque.

Only once during the entire period of observation the left visual acuity had diminished to 0.8 (during the fifth month). After this it rose steadily until it reached 1.5-2 again after a period of two years.

The pericentral scotoma remained but was smaller than originally. Also its connection by an area of relative scotoma with a slight peripheral indentation in this sector remains to the present time.

The retinal lesions disappeared and only a grayish-white sheathing of the three branches of the superior retinal artery near their division remains up to date.

The findings in this case, namely the focal arteriolitis, the cotton-wool areas indicating ischemic infarcts, the hemorrhage, and the subjective findings of a sector-shaped visual field defect with continuous good visual acuity, so similar to those of Case 1, which was a typical Jensen's disease, suggest a similar pathogenesis for Case 2. The only difference in these two cases lies in the site of the arteriolar disease.

It is also not impossible that a similar pathologic process may affect the central retinal artery beyond its ophthalmoscopically visible course, which would produce the picture of a retrobulbar neuritis. In fact, any retinal arteriole could become similarly affected, but would produce a less characteristic subjective and objective clinical picture with a more peripheral location.

Summary and Conclusions

1. Analysis of the clinical findings in Jensen's juxtapapillary retinopathy and comparison with analogous findings occurring in conditions of known pathogenesis suggest overwhelmingly that it is a focal occlusive arteriolar disease of the retina and not a juxtapapillary chorioretinitis or a retinal neuritis.

2. Focal retinal vascular lesions of obscure origin, such as characterize Jensen's retinopathy, in severely allergic or sensitized individuals could be caused by a lowered resistance of the interfibrillary ground substance of their tissues to noxious agents on a constitutional basis, similar to that found in the systemic collagen disorders, only with local manifestations.

3. The main focus of arteriolar disease may have a juxtapapillary location or it may be atypical and have an intrapapillary site. In the former, the diseased arterioles may be buried within the edematous retina and be invisible during the acute stage. In that case, only the cotton-wool areas (ischemic infarcts) suggest the vascular nature of the disease.

4. A similar involvement of the central artery beyond the region of ophthalmoscopic visibility could conceivably produce the picture of a retrobulbar neuritis and should be

included in the differential diagnosis of this disease.

5. Clarification of the concept of Jensen's juxtapapillary retinopathy is of practical therapeutic importance. While ACTH and the steroid hormones may be contraindicated in patients with marked tuberculous allergy, they would be the treatment of choice for all other patients including those in whom no etiologic factor can be found.

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FOOTNOTE

Both patients discussed in this paper were seen before the advent of steroid hormone therapy.

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PIGMENTARY RETINAL LIPOID NEURONAL HEREDODEGENERATION* (SPIELMEYER-VOGT DISEASE)

THE NEURO-OPHTHALMOLOGIC CONSIDERATIONS

JULIUS HOFFMAN, M.D.
Columbus, Ohio

There can be no doubt about the value of ophthalmoscopy in the understanding of neurologic disorders. Indeed, the identification of many such diseases is almost entirely dependent on the presence of characteristic eye findings which are so individual as to be considered pathognomonic. One entity which exemplifies this fact most exquisitely is Spielmeyer-Vogt disease, which is also known as Batten-Mayou disease, juvenile Tay-Sachs disease, juvenile amaurotic family idiocy, and cerebromacular dystrophy.

Though in 1826 Stengel described cases resembling amaurotic family idiocy, in 1881, Warren Tay and, six years later, Bernard Sachs, independently, presented detailed clinical, ophthalmologic, and pathologic studies of the disease which subsequently has been called by their combined names. Typically, the disease symptoms present themselves shortly after a normal birth and are manifested by a progressive mental deterioration, blindness with "cherry-red spot macula," optic atrophy, and convulsive seizures in children of preponderantly, though not exclusively, Jewish families. The termination is invariably fatal within the first two years of life. The clinical description is surpassed in constancy only by the confirmatory microscopic neuropathology.

A primary pathologic alteration is to be found in the ganglion cell where there is a laying-down and accumulation of a lipoid material of uncertain composition such that the neurofibriles and normally remaining nucleus are pushed eccentrically. The usually scalloped outline becomes ballooned or teardrop shaped. This ganglionic change is universal in the cortex, spinal cord, mesentery plexus, and retina. Because of this, and since within the retina the ganglion cells are most numerous in the macula region, a most significant ophthalmoscopic alteration will be noted there. The ganglion pile-up gives a grayish halo surrounding a bright cherry-red spot which is due to the visualization of the choroidal blood vessels at the fovea where there are few or no ganglion cells.

In 1897, Higier and, in 1903, F. E. Batten noted a very similar picture in individuals of a slightly older age group and with certain differentiating features, which were further detailed by Vogt and Spielmeyer in 1905. These studies gave impetus for further investigation of so-called "cerebral lipoidoses" and have brought about not only a further classification and description but also detailed investigations of their relationship to such systemic lipoidoses as Niemann-Pick's disease, Hand-Schüller-Christian disease, Gaucher's disease, and xanthomatosis.

On the basis of intensive research and critical analysis of the numerous papers on the subject, as well as independent clinical and laboratory studies, it is my feeling and that of my co-workers that, indeed, Spielmeyer-Vogt disease is a separate and distinct entity, not only from the systemic lipoidoses but also the infantile type of Tay-Sachs disease. Further, it is felt that the differences far exceed the resemblances which are superficial at best.

Clinically, Spielmeyer-Vogt disease is manifested by an heredofamilial predispo-

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* From the Columbus State School. This paper represents one section of the multiphasic investigation done with Dr. John P. Riepenhoff at the Columbus State School, Columbus, Ohio, and presented at the American Academy of Neurology meeting at Houston, Texas, April, 1955, and the American Association of Mental Deficiency meeting at Detroit, Michigan, May, 1955.

sition as a Mendelian recessive in families of no particular ethnic segment. The prenatal, birth, and the immediate postnatal histories are within normal limits. About the fifth to eighth year of life there are suggestive symptoms indicating visual impairment. After an intellectual arrest, there is an almost precipitous drop to profoundly low levels. Organic psychologic changes, such as irritability, apathy, and speech abnormalities, accompany this decline and are associated with numerous indications of a deteriorating central nervous system. Upper and lower motor neurone palsies, with or without grand mal and/or Jacksonian convulsions, are observed in varying combinations and permutations.

Perhaps the most pathognomonic clinical observations are to be noted in a neuro-ophthalmic sphere. Of no particular or predictable time sequence, pupillary alterations are noted and can be of almost any variety and in association with variable types of strabismus and/or nystagmus. One of the earliest changes observable on ophthalmoscopy is a yellowish-gray appearance of the retina, with slightly narrowed blood vessels. Gradually, small pigmented granules make their appearance at the periphery and in the course of time, proceed centrally, eventually giving the entire retina an appearance resembling retinitis pigmentosa. Shortly after these changes have begun to show up, a macular alteration is noted and with it an expanding central scotoma.

In sharp contrast to the "cherry-red spot" macula of Tay-Sachs disease, in Spielmeyer-Vogt disease there is a central brownish, brick-red core at the macula region. This is surrounded by a pale ring and then a halo of peppery pigmentation. The disc itself becomes extremely pale and presents a primary atrophic picture only late in the progress of retinal alterations.

Except for some, as yet unexplained, lipoid staining differences, the cerebral and spinal pathology in Spielmeyer-Vogt disease and Tay-Sachs disease is morphologically essentially similar. The great difference is in the microscopic pathology of the retina. Thanks to the excellent studies by Greenfield and Holmes, and Ichikawa, et al., it can be concluded that, as a matter of fact, it is because of the retinal pathologic pictures that a different diagnostic category must be established.

The various theories of retinal alteration are well described, including the concept offered by some that retinal changes are due primarily to degeneration of the neuroepithelium with secondary proliferation and regressive changes in the pigment epithelium. Others believe that all retinal neuronal components degenerate uniformly. A third group hypothesize that the first defect is in the rods and cones and the outer nuclear layers with secondary changes in the pigment cells. Three groups have thus compiled these data:

1. Cases in which only the outer layers of the retina suffer and the changes in the inner layers are probably secondary.

2. Cases with changes in the inner layers, especially the ganglion cells, sometimes associated with rods and cones.

3. Cases in which all layers are severely degenerated.

It was felt therefore that the retinal changes are the result of a primary change in the ganglion cells combined with independent degenerations of the outer neuronic elements of the retina which in some cases extend to the inner nuclear and inner reticular layer. This degeneration is followed by a glial sclerosis and proliferation of pigment epithelial cells which wander into degenerated tissue. Involvement of the outer layer distinguishes the retinal lesion of the juvenile from the infantile type of the familial amaurotic idiocy.

The prime alterations observed in Spielmeyer-Vogt disease or Batten-Mayou disease are marked degeneration of the rods and cones as well as the ganglion cells which are less affected than in infantile Tay-Sachs disease. These show vacuolation and appearance of fine brick-red brown pigmentation frequently as the first pathologic sign around the gray-white central macular area. Occa-

sionally the bone corpuscular pigment, peripheral scattering, the delay or even absence of optic atrophy, and the almost universal lack of a cherry-red spot serve as further differential diagnostic points.

There are many changes noted in the pigment epithelium, including an irregular loss within the cells, scattering among the rods and cones resulting in flattening of these pigment cells, poor and irregular arrangement with the nuclei of these cells varying in appearance at both ends of the scale. The nerve-fiber layers of the neuroglial elements replace the degenerated layers. Gradually there is edema of the internuclear layer, then disappearance of the outer nuclear layer, rods and cones, and finally pigmentation.

The retinal blood vessels are often markedly attenuated, although the choroid appears normal. There is also some questionable splitting of the elastica of these blood vessels. There have been case descriptions in which typical pathologic changes were noted in the brain but not in the retina. It was speculated that the reverse might be observed within certain families or that there might be combinations. However, it has been definitely established that pure macular and pure cerebral forms never co-exist in the same families.

Case histories

Two sisters, Bonnie Z., aged 13 years, and Lynn Z., aged 11 years, are the oldest of four siblings, the youngest of whom, Angela Z., aged five years, and Sharon Z., aged three years, are presently apparently entirely well except for slightly abnormal electroencephalograms. The history is that in this Scotch-Irish-German family there is an 18-year-old male cousin who is mentally retarded because of undetermined reasons. There is also a paternal great-half aunt who, supposedly, was normal until her thirties, when she gradually lost her vision and ability to walk. In addition, she became mentally retarded and just recently had her first grand-mal convulsion.* Remaining members of the family appear to be entirely normal, including the parents whose clinical, neurologic, and electroencephalographic examinations are entirely normal.

The prenatal and birth histories of both girls are well within normal limits. It was at about the sixth year of age that the earliest mental abnormalities became manifest. Abstract thinking became impaired and the intellectual decline became so rapid that both had to be withdrawn from the second grade and could not advance, even with private tutoring.

From an above average I.Q. at five years of age both dropped to about 10 at the 11th year when they were admitted to the Columbus State School (Angela's I.Q. is 122 and Sharon's, 130). Both children became withdrawn, irritable, and apathetic. They showed stereotyped behavior as well as paraperceptual (for example, hallucinations) and paracognitive (delusions) symptoms. These symptoms were followed by grand-mal convulsions precipitated by a febrile illness and were associated with petit-mal seizures, stammering, and hesitancy of speech. Echolalia and perseverations soon appeared.

Visual impairment was manifested initially by night blindness and difficulty in color discrimination. Visual acuity decreased and in the older girl is just about nil at present. Ophthalmoscopic examination reveals the classically described alterations in both children with the lesion far more advanced in the older girl whose optic discs are quite atrophied and the blood vessels thread-like (fig. 1†).

Because so little is known about the pathogenic process in this disease, a complete laboratory study of the body organs was

* From the data available one might strongly consider this to be a possible case of Kufs' type of adult familial amaurotic idiocy. Careful investigation is under way to determine if, indeed, this is so. If it is, it might provide a valuable clue as to the relationship of Spielmeyer-Vogt disease to Kufs' disease. A more detailed report is being prepared.

† Direct Kodachrome retinoscopy by Dr. Jack Prince of the Department of Ophthalmology, Ohio State University, College of Medicine. Further ophthalmologic confirmation was given by Dr. William Havener of the same department.

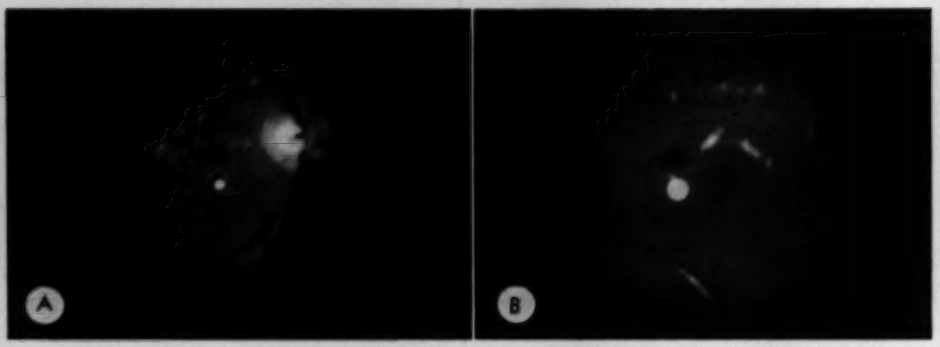

Fig. 1 (Hoffman). Pigmentary retinal lipoid neuronal heredodegeneration. (Direct Kodachrome retinoscopy.) (A) Primary optic atrophy with markedly attenuated blood vessels. (B) Macular pigmentation. (See text for detailed description.)

done. A pneumoencephalograph revealed only slight cortical atrophy in the frontal regions. An electroencephalogram revealed diffusely abnormal patterns, while electrophoretic studies of the serum and spinal fluid are as yet by no means conclusive. Liver, pancreas, thyroid, kidney, adrenal, and bone-marrow functions were all entirely normal. Studies of fat metabolism revealed absolutely no abnormality. High dosage of ACTH administration showed normal responses and prolonged administration of this drug brought about the expected complications (acne, glycosuria, and hypertension), as well as some other (electroencephalogram) changes. However, no significant alteration in the ophthalmoscopic picture was detected.

Discussion

The question of nosologic identification has been brought up frequently in the literature. It is my suggestion that a more appropriate, accurate, understandable, and meaningful name for this entity would be "lipoid neuronal pigmentary retinal heredodegeneration." First of all, it would eliminate the proper name confusion (Spielmeyer-Vogt, Batten-Mayou, Stengel, and so forth). Next, it would separate this disease entity from the group of amaurotic family idiocies, since, technically speaking, it is a dementia rather than an amentia, as implied by the term idiocy. This new name would also do away with the limitation of the incomplete term "cerebromacular dystrophy." The name herein suggested indicates that the disease is a degenerative process of an hereditary nature and involves the neuronal elements wherever they may be and is associated with an inclusion lipoidal deposit of whatever origin. Furthermore, it presents another distinguishing feature, namely, the involvement of the pigmentary, as well as the neuronal, elements of the retina.

Conclusion

Two cases of so-called Spielmeyer-Vogt disease are presented. Several clinical and laboratory studies were performed in an attempt to shed some light on the pathogenic processes. It is felt that this is not a systemic lipoidosis but rather one involving the nervous system, that it is not basically related to Tay-Sachs disease. A more accurate and appropriate nosologic identification "lipoid neuronal pigmentary retinal heredodegeneration" is suggested.

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THE OCULAR MANIFESTATIONS OF LETHAL MIDLINE GRANULOMA*
(WEGENER'S GRANULOMATOSIS)

WILLIAM M. CUTLER, M.D., AND IRVING M. BLATT, M.D.
Ann Arbor, Michigan

Lethal midline granuloma, a disease of unknown etiology, is characterized by an inflammatory granulomatous process involving the upper respiratory tract and progressing to ulceration and gangrenous necrosis of the soft and osseous tissues. Because of greater awareness on the part of the physician, as well as improved diagnostic facilities, this entity is being recognized with increasing frequency.

The ophthalmologist has a definite interest in this disease because of its frequent involvement of orbital tissues. A review of the literature reveals 97 cases of the disease, 38 of these showing ocular involvement (table 2). The majority of authors referred only casually to the ophthalmologic manifestations, and it is possible that other authors omitted them entirely. Only Staehelin,[1] in 1942, has reported ocular histopathology. The purpose of this paper is to present the clinical ophthalmologic details of two cases, to describe the ocular histopathologic changes, cite 11 other unreported cases, and to correlate the ophthalmic findings in their proper perspective.

McBride,[2] in 1896, was the first to describe lethal midline granuloma. In 1933, Stewart[3] described three clinical stages of the disease: (1) Prodromal nasal symptoms, (2) active disease with ulceration and soft and osseous tissue destruction of the midline facial area and the upper respiratory tract, and (3) the terminal stage with exhaustion and hemorrhage. The diffuse systemic form of lethal midline granuloma was described by Wegener[4-5] in 1936 and 1939, and is referred to as Wegener's granulomatosis. This complex is characterized by a necrotiz-

* From the Departments of Ophthalmology and Otorhinolaryngology, University of Michigan Medical School, and the U. S. Veterans Administration Hospital. Pathology reports through the courtesy of the Armed Forces Institute of Pathology.

ing granulomatous angiitis involving the upper respiratory tract, lungs, kidneys, and other organs.

The diagnosis of lethal midline granuloma is made by biopsy and by exclusion of specific diseases. The granuloma contains foreign-body giant cells, eosinophils, plasma cells, and mononuclear cells, with purulent foci of necrosis. Angioblasts, fibroblasts, and necrotizing vasculitis are present.

The etiology is not yet known; however, the granulation tissue may resemble that of the chronic infectious granulomas, including syphilis, Boeck's sarcoid, allergic granuloma, Loeffler's syndrome, periarteritis nodosa, and allergic angiitis and granulomatosis.

Many therapeutic regimens have been used in the past without evidence of definite value. These have included chemotherapy, antisyphilitic therapy, fever, and X-ray therapy. The anti-inflammatory properties of the adrenocortical steroid hormones appear at least to impede the relentless course of the disease.

Case reports

Case 1

C. B., a 35-year-old white man, a conservation officer, noticed a persistent, fetid, sanguinopurulent nasal discharge in May, 1951, with epistaxes occurring up to 12 times daily. Episodic migratory polyarthralgia also began in May, 1951; this was controlled by sodium salicylate. Sixteen months later, the patient noted the onset of bilateral frontotemporal headaches, gradual loss of olfactory function, and decreased gustatory discrimination. Subsequently the patient developed a bilateral suppurative otitis media.

In November, 1953, two and one-half years after the onset of symptoms, ocular manifestations were first noted, characterized by daily episodic aching and fullness in the left orbit associated with conjunctival discharge and photophobia. Constitutional symptoms, including weakness, night sweats, lightheadedness, and nonproductive cough, were also noted. At this time, the patient was admitted to University Hospital for diagnosis and treatment.

On admission to the hospital the patient was pallid and appeared to be chronically ill. There was a musty-odored, profuse, pink, purulent discharge from the nose with blood clots in each nasal chamber. A thick, creamy discharge came from each middle meatus and there was a granulomatous process on the mucous membrane of the anterior portion of the nasal septum and of each inferior and middle turbinate. Neurologic findings included anesthesia of the upper eyelid, nose, and malar eminences bilaterally. Ophthalmologic examination including visual fields was normal; visual acuity was 20/20.

Roentgenographic studies of the paranasal sinuses showed marked clouding of the maxillary, ethmoid, and frontal sinuses. There was evidence of destruction of the cartilaginous and bony septum and inferior and middle turbinates. The chest X-ray film showed a six m. "snowball" nodular density at the base of the left lower lung field. Repeated urinary studies revealed albuminuria, hematuria, and casts.

Histologic examination of multiple biopsy specimens obtained from the nose revealed vascular pyogenic granulation tissue with many eosinophils and foreign-body giant cells. A thorough diagnostic investigation revealed no specific disease, and a diagnosis of Wegener's granulomatosis was made by exclusion.

Soon after ACTH therapy was started the epistaxes ceased, the nasal granulation tissue diminished, and the pulmonary mass decreased in size and density. The renal and joint manifestations also cleared.

Following a three-month period of relatively good health, the patient suffered an exacerbation in March, 1954. He was readmitted to the University Hospital with the complaints of aching upper teeth, anesthesia of the right leg, headaches, and pain in the left eye and ptosis. The visual acuity was still 20/20. The pupils reacted slightly to light. Exophthalmometry at baseline 107 was

Fig. 1 (Cutler and Blatt). *Case 1.* Terminal stage of the disease. Note the saddle-nose deformity. There is proptosis, amaurosis, and conjunctival chemosis. (University Hospital.)

21 mm. bilaterally. There was complete left ptosis and external ophthalmoplegia, except for the torsional action of the superior oblique muscle. There was resistance to compression of the left globe. Funduscopic and field examinations were normal.

Two days later, the vision in the left eye decreased to 20/200 and there was moderate chemosis of the conjunctiva. The left fundus showed a slight suggestion of striae in the macula, but was otherwise normal. The visual field showed a monocular inferior field defect.

After an interval of five days, there was no longer even light perception by the left eye. There was a wide perforation of the nasal septum with a saddle-nose deformity, and paranasal sinus X-ray films showed sphenoid sinus involvement. Increase in density of the chest lesion was seen, and a mottled density was noted in the right lower lung field. The clinical impression was that of granulomatous invasion into the cavernous sinus with involvement of the left orbit and base of the brain.

The dose of ACTH was increased, with the result that in April the patient could again see moving objects with the left eye. In May, however, light perception was again lost. The patient complained of blurred vision and bilateral ocular pain in May, 1954, five months after the first admission. Vision in the right eye was 20/15—2 corrected.

The right pupillary reactions were normal. The left pupil reacted consensually, but only slightly to direct stimulation. The extraocular muscle movements were impaired, but there was much improvement in the left eye. However, for the first time there was impairment of motility of the right eye.

Surgical decompression of the right orbit was considered to prevent further visual loss, but the operation was not done in view of the previous rapid progression of the granulomatous process following a surgical procedure in the late stages of lethal midline granuloma. There was conjunctival hyperemia of the left eye and the proptosis had increased to 22 mm. The first positive

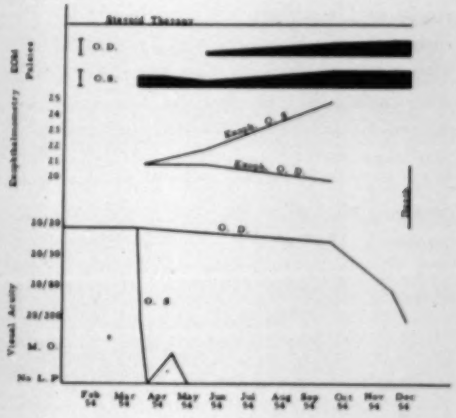

Fig. 2 (Cutler and Blatt). *Case 1.* Course of disease.

funduscopic findings appeared as pallor of the left disc and loss of fine capillarity.

The patient was hospitalized again in August, 1954, because of generalized weakness and hazy vision in the right eye since June, with swelling of the upper lid for three days. The vision in the right eye was 20/25 and J11. No pupillary reactions were noted. Exophthalmometry revealed an increase to 25 mm. in the left eye. There was marked conjunctival chemosis with six to eight mm. of conjunctiva exposed below the cornea. There was now total ophthalmoplegia in the left eye, and only slight lateral motion of the right eye. Neurologic examination revealed involvement of cranial nerves: I through IV, and VII through X bilaterally, V incomplete bilaterally, and VI mainly on the left.

Two months later the ACTH dosage was increased, and Compound F was given orally; the patient received a course of nitrogen mustard and paraminobenzoic acid therapy but the disease progressed relentlessly.

In November, 1954, right visual acuity was 20/80. There was marked proptosis which was more severe in the left eye. There was bilateral conjunctival chemosis, also more severe on the left. The left cornea showed beginning marginal necrosis superiorly and inferiorly. By confrontation the right field was limited to small central vision. The vision in the right eye decreased to 20/200 during the month. At this time the corneal necrosis was more marked and there was also marked cloudiness of the cornea. Two days later the patient's pulse and temperature rose precipitously; he died on December 1, 1954, at the Veterans Administration Hospital, 43 months after onset of the illness.

Ocular pathology Case 1

On enucleation of the left eye at necropsy, Tenon's capsule and the extraocular muscles were difficult to identify. There was a firm, yellowish-white granulation tissue filling the entire orbit, inside the muscle cone, and adherent to the optic nerve and posterior pole of the globe.

The following report is from L. E. Zimmerman, M.D., Armed Forces Institute of Pathology:

"Centrally there is ulceration of the corneal epithelium and partial destruction of Bowman's membrane. Toward the periphery, the epithelium is intact but appears atrophic. The subepithelial tissues at the periphery are intensely infiltrated by chronic inflammatory cells with lymphocytes predominating. There is marked vascularization of the corneal stroma at the periphery and extending into the central areas. The stroma is diffusely infiltrated by polymorphonuclear leukocytes and this infiltration involves all layers, but is most intense centrally where the epithelium is ulcerated. Descemet's membrane is intact and the corneal endothelium is edematous.

"An increased number of nuclei are observed in the corneoscleral trabeculas and the intertrabecular spaces appear somewhat compressed. A few inflammatory cells are seen about the canal of Schlemm and these include large histiocytic elements. The anterior chamber appears to be of normal depth and there is no hypopyon. There is increased prominence and size of the endothelial cells lining the anterior surface of the iris, and in the pupillary zone there are also large mononuclear elements which infiltrate the anterior iris stroma. Similar cells, less densely packed, are seen in the more peripheral portions of the iris stroma. These cells resemble tissue macrophages. Lesser numbers of small mononuclear cells, chiefly lymphocytes, are also seen in the iris stroma.

"The ciliary muscle is atrophic and edematous. Cells, similar to those observed in the iris stroma, are present in the stroma of the ciliary body. There is light but diffuse infiltration of lymphocytes throughout the choroid, and lesser numbers of other inflammatory cell types are also seen. The most striking choroidal change, however, is

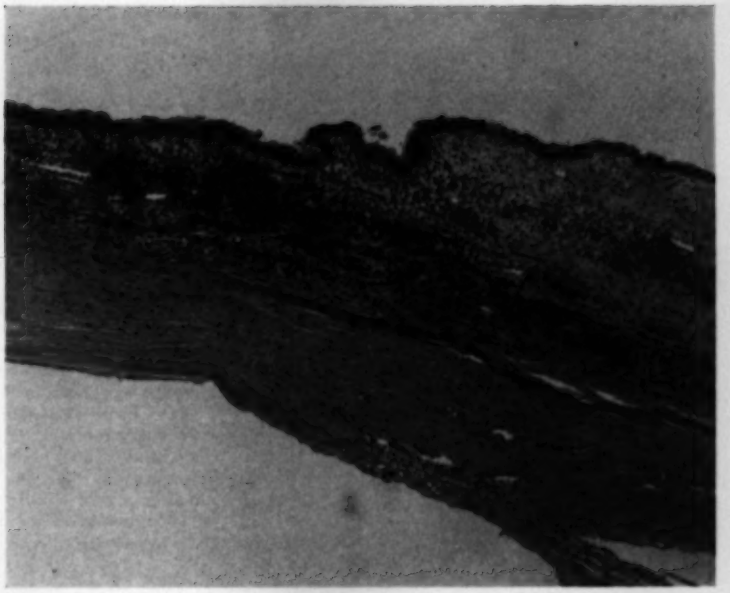

Fig. 3 (Cutler and Blatt). Peripheral cornea. The subepithelial tissues are intensely infiltrated by chronic inflammatory cells, with lymphocytes predominating. There is marked vascularization of the corneal stroma. The stroma is diffusely infiltrated by polymorphonuclear leukocytes. The corneal epithelium is edematous. (Hematoxylin-eosin. ×100. AFIP Acc. 684869.)

Fig. 4 (Cutler and Blatt). Angle of the anterior chamber. Cellular infiltration is around the corneoscleral trabeculae and the canal of Schlemm, including large histiocytic elements. The intertrabecular spaces appear somewhat compressed. Large endothelial cells line the anterior surface of the iris. Small mononuclear cells and large cells resemble tissue macrophages in the stroma. The ciliary muscle is edematous and atrophic, and similar inflammatory cells are present. (Hematoxylin-eosin. ×100. AFIP Acc. 684869.)

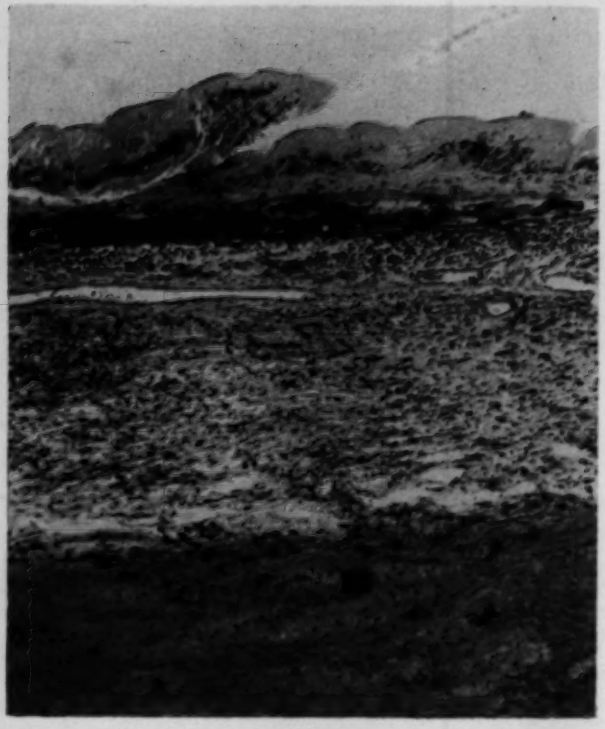

Fig. 5 (Cutler and Blatt). Retina and choroid. There is mainly lymphocytic infiltration throughout the choroid, and marked sclerosis of choroidal blood vessels. The choroid is thickened due to interstitial edema and fibrosis. There is extreme proliferation and metaplastic change in the retinal pigment epithelium, and in other areas it appears necrotic. The sensory retina is also markedly degenerated. (Hematoxylin-eosin, ×100. AFIP Acc. 684869.)

the presence of marked sclerosis of the choroidal blood vessels. This sclerosis involves thickening of the media without significant intimal proliferation. The endothelial cells lining these vessels, however, are plump and prominent. There is also marked choroidal thickening due to interstitial edema and fibrosis. There is a severe disturbance of the retinal pigment epithelium which, in large areas, appears necrotic, while in other areas, especially posteriorly, it shows extreme proliferation and metaplastic change. Associated with these changes are marked alterations in the sensory retina. Only at the periphery is the retinal architecture fairly well preserved. Elsewhere, there are areas of chorioretinal scarring, other areas of extensive necrosis of the retina, and still other areas of retinal detachment.

"There is marked fibrosis in the region of the lamina cribrosa and posterior to this the optic nerve shows an extreme degree of atrophy. Further back, the optic nerve shows a coagulative type of necrosis involving the nerve bundles and an extreme proliferation of microglia in the necrotic nerve tissue. The central retinal artery appears collapsed while the vein shows evidence of thrombosis with recanalization. A necrotizing inflammatory process involves the sheaths of the optic nerve as well as the orbital tissues and episclera. There are many areas of tissue necrosis heavily infiltrated by polymorphonuclear leukocytes. The reaction appears most severe in the orbital fat. Adjacent to these areas arterioles showing marked intimal proliferation are observed and there are dilated venules lined by prominent endothelium."

Case 2

S. O., a 51-year-old housewife, experi-

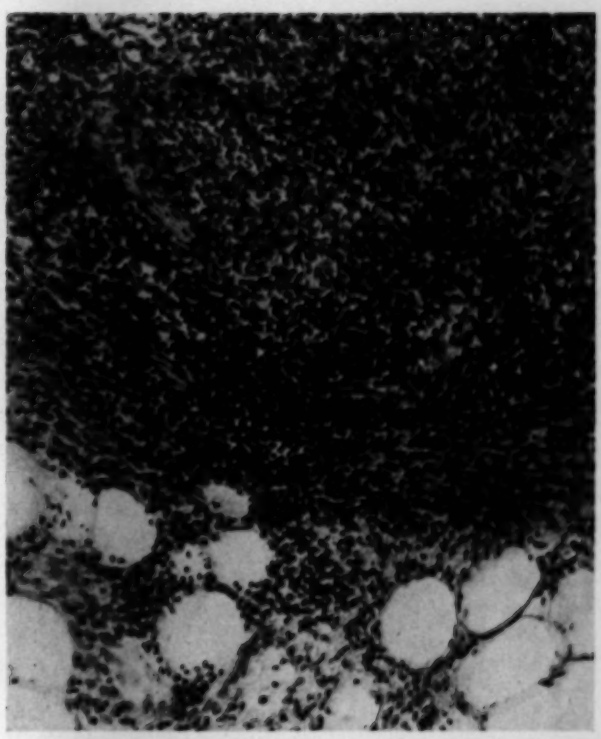

Fig. 6 (Cutler and Blatt). Granuloma in episclera adjacent to optic nerve. There are many areas of focal necrosis heavily infiltrated with polymorphonuclear leukocytes. Adjacent to these areas the arterioles show marked intimal proliferation. Orbital fat is seen below. (Hematoxylin-eosin. ×250. AFIP Acc. 684869.)

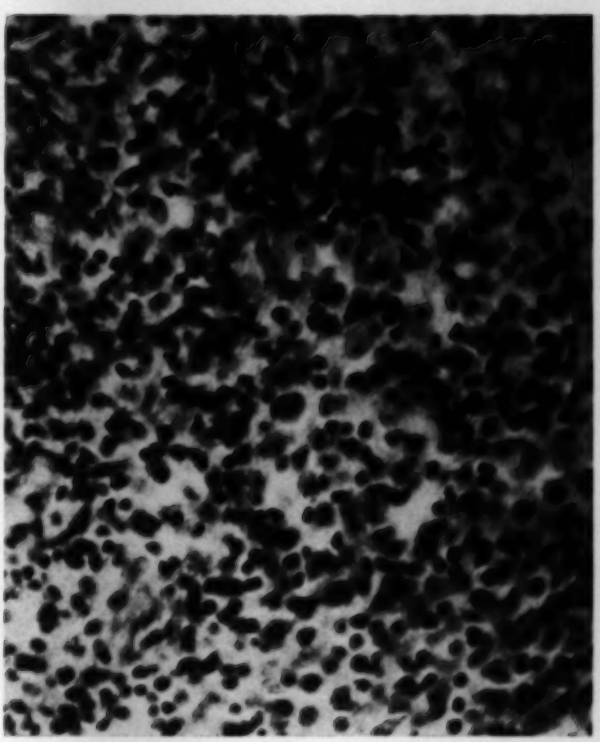

Fig. 7 (Cutler and Blatt). High-power view of granuloma in episclera. The whorled mass contains mononuclear cells, epithelioid cells, and some polymorphonuclear leukocytes. (Hematoxylin-eosin, ×800. AFIP Acc. 684869.)

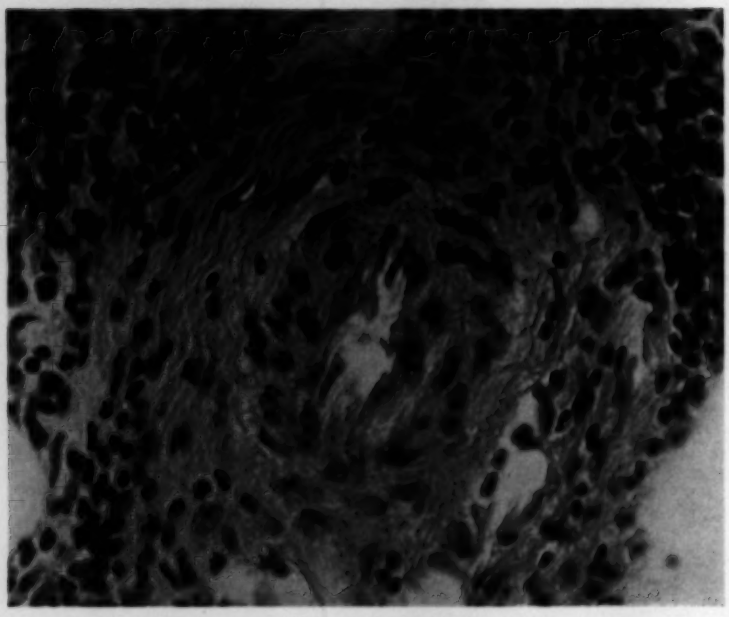

Fig. 8 (Cutler and Blatt). High-power view of an arteriole in the granuloma shows marked intimal proliferation. (Hematoxylin-eosin. ×1000. AFIP Acc. 684869.)

enced nasal stuffiness and a serous nasal discharge for 25 years; since 1935, she had been a mouth breather. A purulent nasal discharge was noted in 1952 and episodic migratory polyarthralgia began in February, 1953. Because of the profuse nasal discharge and obstruction, the patient underwent a nasal polypectomy in April, 1953. The operative site failed to heal, and the purulent nasal discharge persisted until the patient's admission to this hospital. One month after the nasal operation the patient developed a pneumonitis and a bilateral suppurative otitis media. At this time she noted pain in the maxillofacial area and the onset of anorexia, night sweats, weight loss, and weakness.

Examination in September, 1953, revealed a nasal septal defect with granulation tissue and crusting. There was a purulent discharge from the ears, with a severe conductive hearing loss. Urinalysis showed cylindruria, hematuria, and albuminuria.

The chest X-ray film showed a nodular density in the right lower lung field and a nodular density with cavitation in the left upper lobe. There was clouding of the maxillary and ethmoid sinuses and thickening of the nasal mucous membrane.

The ophthalmic examination was normal. Nasal biopsies showed necrotizing granulation tissue with Langhan's type giant cells. Extensive diagnostic studies revealed no specific disease, and a diagnosis of Wegener's granulomatosis was made by exclusion. Steroid therapy was started in September, 1953, with marked improvement of the nasal obstruction, hearing, and regression of the pulmonary lesions.

In April, 1954, the patient had excessive lacrimation and difficulty in focusing for reading. The visual acuity was 20/30. There was epiphora, and the medial canthi were very tender to pressure. The fundi were normal with many drusen in the periphery.

The patient soon noted the onset of diplopia, especially marked on downward gaze. In August, 1954, proptosis of the left

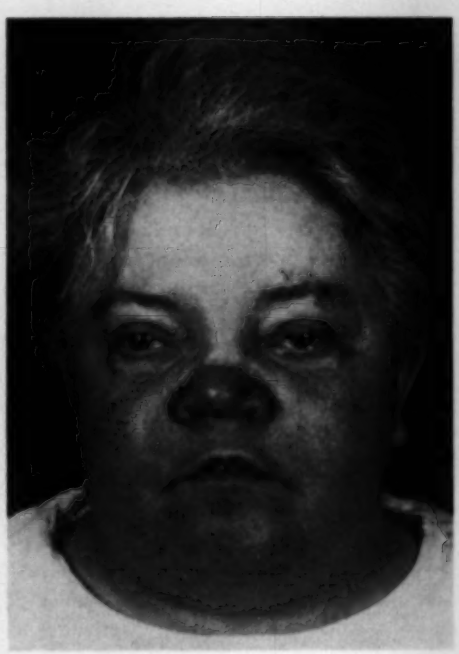

Fig. 9 (Cutler and Blatt). *Case 2.* Fulminating stage before remission. Note saddle-nose deformity. The moon facies is due to steroid therapy. There is proptosis, amaurosis, and optic atrophy. (University Hospital.)

eye developed, and there was pain over the entire face and particularly beneath the eyes. At this time the visual acuity was 20/50 and reading was J7 and J11. The exophthalmometry at baseline 105 was 17 right and 19 left. There seemed to be a slight left ptosis and the palpebral fissures measured eight mm. and seven mm. Red-glass diplopia denoted paresis of the left medial rectus muscle, and there was moderate chemosis of the left conjunctiva with slight engorgement of vessels in the inferior cul-de-sac. The pupils and fundi were normal. The visual field examination showed some constriction. The epiphora had subsided.

In September, 1954, the steroid level had to be increased, and following this the ocular symptoms were slightly better, with no diplopia. Visual acuity was still 20/50. The exophthalmos had decreased to 15.5 and 18.5 mm., and the conjunctival chemosis and paresis of the left medial rectus muscle had disappeared.

In October, 1954, a bleeding duodenal ulcer developed secondary to steroid therapy, and the patient was placed on a medical ulcer regimen. The steroid medication was decreased, with the result that the patient had an exacerbation with marked decrease in vision, especially in the left eye, and an increase in retrobulbar and facial pain.

X-ray examination of the paranasal sinuses showed erosion of the walls of the sphenoid sinuses.

Vision in the right eye was 20/200, and there was only light perception in the left. The left pupil was more miotic than the right; both pupils reacted slightly to light. Proptosis was more evident in the left eye, with decreased orbital compressibility. Both lids were puffy. There was exotropia in the primary position and the extraocular movements were limited.

A few weeks later there was no longer light perception in the right eye; the left eye detected light and moving objects. There was almost complete bilateral ophthalmoplegia, with only slight motion of the left eye. The exophthalmos had increased to 18 and 22 mm. Three weeks later the patient

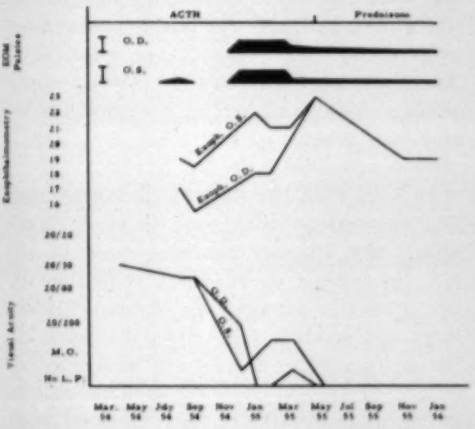

Fig. 10 (Cutler and Blatt). *Case 2.* Course of the disease.

was able to count fingers with the left eye, at four feet. There was still right exotropia of about 20 degrees, and partial external ophthalmoplegia. The proptosis of the left eye measured one mm. less. Minimal conjunctival chemosis was noted, and early primary optic atrophy in the right eye, which was the first positive funduscopic finding.

Two months later the patient became weaker and required increased doses of narcotics, but she recovered light perception and vision of moving objects on the right, and still had "finger counting" vision on the left. The eyes were straight in the primary position and the external ophthalmoplegia had improved. Slight ptosis, periorbital edema, and chemosis were still evident. The right proptosis had increased from 18 to 20 mm. There was early marginal corneal infiltration. The right fundus showed early optic atrophy, generalized attenuation of the arterioles (grade 2), and some periarteritic lipid infiltration adjacent to the disc. A left visual field was obtained and showed a large, dense, central scotoma. Since the left fundus was normal the change was interpreted as retrobulbar neuritis.

Two months later in May, 1955, the patient again lost light perception in the right eye, and soon afterward that in the left. The lids were now tense against the exophthalmic globes, and were completely ptotic. The proptosis had increased to 23 mm. bilaterally. There was more marked right primary optic atrophy with periarteritic circumpapillaris and very attenuated arterioles; early optic atrophy appeared in the left fundus.

In May, 1955, the form of steroid therapy was changed to prednisone (delta-1 cortisone), and, whether this was incidental or not, the patient underwent a remission in her general symptoms. In January, 1956, three and one-half years after the onset of the active disease, the patient was in good general health and had no granuloma visible in her upper respiratory tract. However, she was completely blind, with primary optic atrophy bilaterally. Her exophthalmos had decreased to 19 mm. bilaterally, and she had no ptosis or conjunctival edema, and her extraocular muscle movements were almost full. The marginal corneal infiltration persisted on the right.

University of Michigan Hospital cases

Thirteen cases of lethal midline granuloma are listed in Table 1. This includes the detailed Cases 1 and 2. Eight of the 13 cases have concurrent ocular pathologic changes.

Review of the literature

The ocular findings in reported cases of lethal midline granuloma are summarized in Table 2.

Discussion

Lethal midline granuloma affects the ocular tissues in 42 percent of the total reported cases. Its ocular lesions are often similar to an extraocular orbital tumor originating at

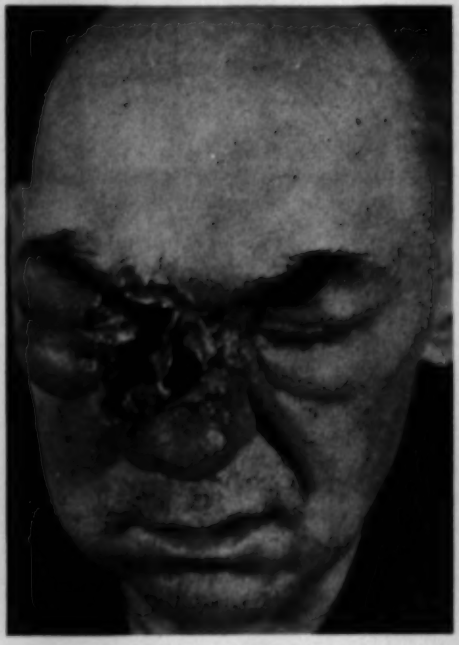

Fig. 11 (Cutler and Blatt). *Case 9* (table 1). The terminal stage. (University Hospital.)

TABLE 1

THIRTEEN UNIVERSITY HOSPITAL UNREPORTED CASES

Case	Patient	Age (yr.)	Race Sex	Early Symptoms	Duration of Disease		Sphenoidal Involvement	Pulmonary	Renal	Joints	Others	Ocular
					Prodromal	Active						
1	C. B.	35	WM	Bloody, purulent discharge	1 mo.	43 mo.	+	+	+	+	CNS	Amaurosis, exophthalmos, chemosis, marginal corneal necrosis, total ophthalmoplegia, ptosis, lid edema, optic atrophy, granuloma in orbit, infiltration in cornea, iris, and choroid. (See case 1.)
2	S. O.	51	WF	Nasal obstruction	19 yr.	3½ yr. living	+	+	+	+	Anemia	Proptosis, EOM palsies, ptosis, chemosis, decreased compressibility, lid edema, amaurosis, optic atrophy, central scotoma, marginal corneal infiltration. (see case 2.)
3	J. D.	57	WF	Cough, epistaxis	1 yr.	4 mo.	+	–	+	–	–	Neg.
4	R. B.	42	WF	Nasal obstruction	3 yr.	1 yr.	–	–	–	–	–	? None
5	C. H.	36	WM	Nasal obstruction	15 mo.	11 mo.	–	–	+	–	–	Lid edema, diplopia, acute dacryocystitis, cellulitis of face
6	E. G.	49	WM	Nasal obstruction stuffiness	5 yr.	16 mo.	–	–	–	–	Anemia	Neg.
7	C. S.	27	WM	Bloody discharge	10 mo.	2 mo.	+	hemoptysis	–	–	CNS	Papilledema, nystagmus, dissociated EOM
8	A. C.	38	WF	Pain, stuffy nose	6 mo.	21 mo.	++	–	+	+	Anemia	Orbital cellulitis
9	J. E.	51	WM	Nasal obstruction	10 mo.	8 mo.	–	–	–	–	Petechial skin rash	Lid edema, large nasal destruction (see Fig. 11)
10	O. W.	31	WF	Weakness, headaches, swollen feet	16 yr.	3 yr., 2 mo.	–	+	+	+	Anemia, eosinophilia, erythema nodosum	Recurrent eczematous keratoconjunctivitis, marginal corneal infiltration
11	A. F.	54	WF	Nasal crusting	?	5 yr.	–	–	–	–	–	Neg., living at age 62 after 2 radical nasal resections
12	F. V.	53	WM	Epistaxes	6 mo.	13 mo.	–	++	++	+	Anemia	? Neg.
13	L. D.	28	WM	Persistent URI, epistaxes	2 mo.	8 mo.	–	–	++	+	Anemia	Episcleritis, marked bulbar conjunctival injection

the apex. The most common findings are proptosis, decreased visual acuity leading to amaurosis, optic atrophy, limitation of ocular motility, ptosis, lid edema, and conjunctival chemosis. The special feature of this granuloma is its necrotizing angiitis, which is seen in the orbit (figs. 6 and 7), and involving the sheaths of the optic nerve (fig. 6). This severe necrotizing reaction around the optic nerve leads to a marked atrophy and coagulation necrosis of the optic-nerve bundles. Clinically a retrobulbar neuritis may precede the amaurosis and primary optic atrophy (Case 2).

There are three likely routes of orbital invasion:

1. The sphenoid sinus—from the involved sphenoidal area the orbital invasion may occur by contiguity through the optic foramen and superior orbital fissure. Of the 13 University Hospital cases (table 1), six had roentgenographic evidence of sphenoid involvement, and five of these clinically had orbital invasion. Case 1 had histologic evidence of granuloma in the orbit and there was sphenoid sinus clouding and bony erosion by X-ray examination, but no osseous defect in the walls of the orbit from any direction at necropsy.

2. Blood and lymph vessels—this process would be similar to that of nasopharyngeal tumors, which are said to invade the orbit through the foramen lacerum, along the internal carotid artery, and into the orbit through the superior orbital fissure.[35]

3. Diffuse inflammation—the orbital invasion may be a separate,

TABLE 2

REPORTED CASES OF LETHAL MIDLINE GRANULOMA

Author	Reference No.	Date	Ocular Disease	No. Cases Reported	No. Cases Ocular Involvement
MacArthur	6	1925	Orbital invasion	1	1
Klinger	7	1931	Proptosis, amaurosis	1	1
Ludtke	8	1931	Lid edema, bony destruction of floor of orbit, necrosis of lids, granuloma on the globe	1	1
Wood	9	1931	Orbital invasion	1	1
Derischanoff	10	1931	Lid edema	1	1
Myerson	11	1933	Ulceration and necrosis of eyelids, sequestration of orbital plate of ethmoid, slough of orbital fat	1	1
Rossle	12	1933	Pyoderma of eyelids, medial and lateral canthal ulcers, corneal ulcer, amaurosis	1	1
Voss	13	1934	Conjunctivitis, corneal ulcer, proptosis, dacryocystitis	2	1
Berendes	14	1934	Lid edema, orbital pain	1	1
Sturm	15	1935	Sequestration of medial orbital wall, edema and ulceration of eyelids, granulomatous invasion of orbital bones, medial canthal ulceration, proptosis, conjunctival chemosis	2	2
Joisten	16	1936	Cellulitis of "eye," infraorbital edema	2	2
Bayer	17	1937	Purulent swelling medial canthus, edema and cellulitis of eyelids, sequestration of orbital plate of ethmoid	1	1
Schutz	18	1938	Ulceration of conjunctiva, ulceration of medial canthus	4	1
Dennie	19	1940	Orbital invasion, amaurosis	1	1
Hoover	20	1941	Necrosis of orbit, lacrimal sac abscess	4	1
Dahm	21	1942	Proptosis, lid edema, perforation of medial canthus, swelling medial canthus, bony distribution of orbital floor, perforation of lacrimal sac	5	4
Staehelin	1	1942	Edema of eyelids, III C.N. paralysis, ptosis, proptosis, central scotoma, amaurosis, optic nerve and its sheaths infiltrated, granuloma in sclera and choroid	1	1
Williams	22	1949	Proptosis, perforation at each medial canthus	3	1
Williams	23	1950	Proptosis, orbital invasion, bony distruction	1	1
Howells	24	1950	Lid edema	1	1
Dahm	25	1950	Dacryocystitis, bony destruction, necrosis medial wall of orbit, infiltration of globe	3	2
McCart	26	1950	Lid edema, proptosis, granuloma of floor or orbit	2	1
Mass. Gen.	27	1951	Keratitis, iritis, uveitis	1	1
Stratton	28	1953	Exophthalmos	2	1

TABLE 2—(*continued*)

Author	Reference	Date	Ocular Disease	No. Cases Reported	No. Cases Ocular Involvement
Castello-Pardo	29	1953	Ulcer of eyelid, lacrimal sac fistula	1	1
Breckenridge	30	1954	Conjunctivitis, ulcerative granuloma of lids, orbital bone destruction, orbital granuloma	5	2
Fahey Godman	31 32	1954	4 proptosis; 1 each corneal ulcer, chemosis, amaurosis, conjunctival congestion, conjunctival petechiae	29	4
Cogan	33	1955	Corneal infiltration with furrow and vascularization	1	1

SUMMARY

	No. Cases Reported	No. Cases Ocular Involvement	Percent
Total of the above cases	79	38	48
Other authors not reporting ocular disease (34)	18	—	—
Total cases in the literature	97	38	39
University of Michigan Hospital Cases	13	8	62
TOTAL KNOWN CASES	110	46	42

noncontiguous granuloma appearing as a manifestation of disseminated necrotizing angiitis in many organs, such as lungs, spleen, and kidneys.

Cases 1 and 2 are very similar in early clinical development of the disease, with amaurosis, optic atrophy, proptosis, and ophthalmoplegia. The patient in Case 2 obtained a remission when therapy was changed from ACTH to prednisone (this may be incidental). Since then the ocular motility improved and the proptosis decreased, but the amaurosis and optic atrophy remained. It appears that the granulomatous process subsided, but the optic-nerve damage was already irreversible.

There is no available ocular histopathology from early and minimal cases of orbital involvement. Case 1 shows the late stages with widespread inflammatory and degenerative changes in almost all the ocular tissues. Palliation and extension of the course of the disease through steroid therapy undoubtedly helped to permit these marked changes to occur.

As seen in Figures 3, 4, and 5, there is infiltration of the conjunctiva, cornea, iris, filtration angles, and choroid with inflammatory cells including large histocytes which resemble tissue macrophages. Clinically there was progressive marginal corneal necrosis in the late stages of Case 1. Case 2 also has marginal corneal infiltration. No clinically evident glaucoma or iritis existed however.

Marked inflammatory and degenerative changes occurred in the choroid and retina (fig. 5). The choroidal vessels showed thickening of the media and prominent endothelial cells.

In the orbital granuloma there was marked intimal proliferation (fig. 8) of the arterioles, and areas of focal necrosis. These latter features of the granuloma are helpful in histologic diagnosis, but in general other disease entities must be ruled out in order to establish a diagnosis of this nonspecific granulomatous process.

Wegener's granulomatosis and lethal midline granuloma are of interest to the ophthalmologist when a differential diagnosis includes orbital tumors and specific chronic inflammation. The following outline combines recommendations made by Duke-Elder[36] and by Reese.[35]

DIFFERENTIAL DIAGNOSIS

A. NEOPLASM

1. Primary orbital
2. Metastatic to orbit
3. Secondarily involving orbit
   a. Nasopharynx and nasal cavity
   b. Paranasal sinuses

B. CHRONIC ORBITAL INFLAMMATION

1. Nonspecific orbital inflammation
   a. Chronic orbital myositis
   b. Nonspecific granuloma or inflammatory pseudotumor
2. Specific chronic inflammation
   a. Glanders
   b. Boeck's sarcoid
   c. Anthrax
   d. Tuleremia
   e. Typhoid
   f. Tuberculosis
   g. Syphilis
   h. Mycotic infections
   i. Parasitic infections
   j. *Lethal midline granuloma*

C. GENERALIZED DISEASE

1. Endocrine disorders (thyrotoxicosis)
2. Lipodystrophies
3. Periarteritis nodosa
4. Lymphoblastoma (leukemia, Hodgkin's disease, chloroma, etc.)
5. *Lethal midline granuloma (Wegener's granulomatosis)*

Duke-Elder[36] classifies nonspecific chronic inflammation of the orbit in two categories: (1) Chronic orbital myositis, and (2) nonspecific granuloma or inflammatory pseudotumor. The latter group is large and ill-defined, representing clinical rather than pathologic criteria for evaluating lesions that resemble orbital tumor. Classification in this group is becoming more definite and restricted as diagnostic facilities improve. Certain cases of chronic granuloma of the orbit that cannot be diagnosed on an etiologic basis may later be classified as a specific entity. Lethal midline granuloma, when diagnosed, can be removed from the category of "inflammatory pseudotumor," as indicated in the above outline, and placed in either the category of specific chronic inflammation or manifestation of generalized disease.

Lethal midline granuloma may be diagnosed by the ophthalmologist after neoplasms and other specific entities are ruled out by tissue study. It is important to note that surgical intervention may cause acute exacerbation in the disease complex; therefore treatment should not be considered until the specific diagnosis is made in any of these conditions. X-ray therapy will not dramatically affect the disease process, as it does in lymphoblastoma.

SUMMARY

Lethal midline granuloma (Wegener's granulomatosis) is a progressive, nonspecific, granulomatous inflammatory process of unknown etiology. The original lesion is usually in the upper respiratory tract, and the orbit, globe, and ocular adnexae may be involved. The clinical ocular picture is essentially that of an extraocular orbital tumor, with additional granulomatous infiltration of various ocular tissues. The prognosis is extremely poor; however, steroid therapy offers some palliation and Case 2 has exhibited a good remission.

University Hospital.

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EXPERIMENTAL SCLERAL SURGERY OF THE MONKEY*

TAYLOR ASBURY, M.D.
Cincinnati, Ohio
AND
DANIEL G. VAUGHAN, JR., M.D.
San Jose, California

Surprisingly little experimental work has been done in the field of retinal detachment surgery. Most of our knowledge has been gained as a result of trial and error on human subjects. A few scattered reports of animal studies have appeared; for example, the report of Dellaporta's work[1] which was chiefly with dogs, but nothing seems to have been done with any of the higher animals such as monkeys.

Dog's sclera, aside from being very thin, is much more vascular than human sclera. The sclera of five- to seven-pound monkeys is also fairly thin but it has about the same vascularity and general composition as human sclera. In the hope of gaining information applicable to human sclera on the basis of this similarity, operations were performed on 14 monkey eyes. Postoperatively these eyes were subjected to fundus study, and then, after enucleation at various postoperative intervals, to careful histologic analysis.

TYPES OF SURGERY PERFORMED

Early in the project an effort was made to compare the lamellar type of scleral resection with the full-thickness operation. Later the scleral buckling operation, as advocated chiefly by Schepens, was studied. Finally, lamellar scleral resection, with and without diathermy, and scleral buckling, with and without diathermy, were also compared. Efforts to produce retinal detachments on which to perform surgery were unsuccessful.

1. LAMELLAR SCLERAL RESECTION

This operation on the monkey eye was designed to correspond to the lamellar scleral resection advocated by Pischel.[2] Intraperitoneal nembutal was found to be the easiest and most effective anesthetic. The sclera was bared in the temporal quadrant. Six mm. behind and concentric to the limbus, a strip one-mm. wide and 10-mm. long was outlined with a No. 15 Bard-Parker blade, and the grooves were carried down approximately three fourths of the way through the sclera. The lamellar strip was then removed with the Bard-Parker blade which was held carefully in the original dissection plane. No. 6-0 black silk sutures were then placed in mattress fashion about one mm. apart. In some cases the remaining lamellar fibers were treated with light diathermy by means of a flat electrode which was passed slowly over the entire lamellar area (Walker diathermy machine set at 25). A paracentesis was performed and the scleral sutures were then tied securely. The conjunctiva was reapproximated and the lids sutured together loosely with catgut.

This operation was performed on five eyes. In three of the five the remaining deep lamellar fibers also received diathermy (table 1). There were no surgical complications but, in one operation, a small bead of vitreous was lost in the placing of one suture. At enucleation on two occasions there was a sudden loss of vitreous due to excessive pressure on the globe. In one of these in-

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TABLE 1

SUMMARY OF PROCEDURES, POSTOPERATIVE COURSES, AND COMPLICATIONS OF SCLERAL SURGERY ON MONKEYS' EYES

Monkey Eye	Procedure	Diathermy + 0	Surgical or Postoperative Complications. Unusual Events, Enucleation, etc.	Postoperative Interval before Enucleation
1	Attempted to produce retinal detachment	0	Unsuccessful. End result: phthisis bulbi	4 wk.
2	Lamellar scleral resection	0	No complications at surgery, postoperatively or at enucleation	3 wk.
3	Lamellar scleral resection	0	No complications at surgery, postoperatively, or at enucleation	6 wk.
4	Lamellar scleral resection	+	One bead of vitreous lost in placing one suture. No other complications	5 days
5	Lamellar scleral resection	+	At enucleation there was sudden loss of considerable vitreous due to excessive pressure on the globe by instruments. This also caused a vitreous hemorrhage. No other complications	1 wk.
6	Lamellar scleral resection	+	Enucleation attempted at 1 week. There was sudden loss of vitreous, as in monkey eye #5. Eye was left in and recovered completely. Enucleated 2 mos. later. No complications	9 wk.
7	Full-thickness scleral resection	0	Sudden loss of small amount of vitreous in suturing. No other complications	2 wk.
8	Full-thickness scleral resection	0	No complications at surgery, postoperatively or at enucleation	5 wk.
9	3 small full-thickness scleral resections	0	No complications at surgery, postoperatively, or at enucleation	2 wk.
10	Scleral buckling	0	Used polyethylene tube that was too large. Slight vitreous loss in placing one suture. No other complications	4 wk.
11	Scleral buckling	0	No complications at surgery, postoperatively, or at enucleation	6 wk.
12	Scleral buckling	+	At sectioning after enucleation, almost complete erosion of polyethyelene tube into vitreous cavity. No other complications	1 wk.
13	Scleral buckling	+	Smaller tube used. No complications	3 wk.
14	Scleral buckling	+	No complications at surgery, postoperatively, or at enucleation	4 wk.

stances (eye 5), the enucleation was completed anyway. Histologic examination disclosed a small vitreous hemorrhage and rupture of the scleral wound. In the other instance (eye 6) the sudden gush of vitreous occurred early in the enucleation before the optic nerve had been severed. The conjunctival wound was closed and the monkey saved. The histologic picture of this eye is presented in detail later.

2. CONVENTIONAL FULL-THICKNESS SCLERAL RESECTIONS

On two monkey eyes the same lamellar

scleral resection technique described above was carried out except that the scleral strip was excised completely with a pair of straight Castroviejo corneal scissors. To avoid vitreous loss, great care was taken not to perforate the choroid. In spite of this effort, however, vitreous loss did occur in the placing of the sutures on one of the two eyes. Diathermy was not used in either of these cases.

3. Small multiple full-thickness scleral resections

In an effort to accomplish scleral shortening in two directions at the same time, so as to reduce the effect of a pulling of vitreous strands in more than one direction, Eye 9 was subjected to three small full-thickness scleral resections. Three scleral strips two-mm. long and one-mm. wide with tapered ends were placed in the temporal horizontal meridian so that the most anterior one was six-mm. behind the limbus. Then two mm. farther back, and also concentric to the limbus, two similar pieces of sclera were removed, one above the other, with the lower end of the upper one two mm. from the upper end of the lower one. At surgery and postoperatively the one eye treated in this way had an uncomplicated course.

4. Scleral buckling

This operation was designed to correspond with the scleral buckling operation advocated by Schepens.[3] The technique was exactly the same as in the performance of lamellar scleral resection except that an effort was made to remove the scleral strip as far back as possible. The anterior edge of the wound was thus at least nine mm. behind the limbus, which would correspond to 15 or 16 mm. behind the human limbus. One-mm. bites were taken in the placement of mattress sutures in the sclera to reduce the tendency of the sutures to pull out. In three of five eyes so treated, the deep lamellar fibers were subjected to light surface diathermy as described above in connection with lamellar scleral resection. A very small polyethylene tube, fitting a No. 25 Luer-Lok needle, was then placed under the mattress sutures over the whole area of resection. A paracentesis was required before the sutures could be tied securely. A tube fitting a No. 19 Luer needle was used in the first eye so treated but was found to be too large. With tubes that fitted a No. 25 needle there were no operative complications but, in one instance, a tube was found nearly eroded into the vitreous cavity when the eye was removed one week postoperatively (figs. 11 and 12).

General response to surgery

Without exception, the monkey eyes did well postoperatively, even when minor complications occurred at surgery. In no case did a retinal detachment develop even though at least two eyes received more than the calculated surgical trauma. (One of these, Eye 6, will be discussed in detail later in this report.) The catgut sutures used in closing the lids and reapproximating the conjunctiva either pulled loose or absorbed in from three to five days, and the conjunctival wounds healed quickly without any special postoperative care.

Postoperative funduscopy

In view of the anesthetic hazard involved in repeated postoperative examinations, funduscopy was kept at a minimum. Every fundus was seen once during the first three-week postoperative period and in all cases the retina was found to be flat in the posterior portion of the eye. The resected areas were for the most part too far forward to be well visualized. These difficulties might perhaps have been somewhat reduced by the use of indirect ophthalmoscopy and scleral depression.

Histologic analysis

In this study the most important information was gained from the histologic findings.

By means of histologic analysis of the enucleated eyes, the effect of the various operative procedures on the sclera, choroid, vitreous, retina, and globe could be evaluated, and certain conclusions, applicable in a limited way to human retinal detachment surgery, could be drawn. The enucleated eyes were fixed in formalin for several days prior to sectioning, and the sections were then stained with hematoxylin-eosin.

A. LAMELLAR SCLERAL RESECTION WITHOUT DIATHERMY (TWO EYES)

Eye 2—enucleated at three weeks.
Eye 3—enucleated at six weeks.

Two eyes were subjected to this operation. The surgery, postoperative courses, and enucleations were uncomplicated. Histologically, a granulomatous foreign-body type of response was manifest by the third week with lymphocytes, epithelioid cells, and foreign-body giant cells in evidence. The silk sutures were responsible for the granulomatous element of the reaction but were tolerated well.

Fig. 1 (Asbury and Vaughan). *Eye 3.* Lamellar scleral resection without diathermy, enucleation six weeks postoperatively, showing artefactual retinal detachment except in area of surgery. (×18.)

The retina, which undergoes rapid post-mortem changes, was recognizable everywhere but showed slightly more atrophy in the immediate area of surgery. The layer of rods and cones, and the ganglion-cell layer, even more particularly, undergo very rapid post-mortem changes no matter how soon the eye is fixed after enucleation. It is significant that in Eye 3, enucleated at six weeks, the retina was artefactually detached except over the area of scleral surgery where it was adherent (fig. 1).

The lamellar scleral resection by itself caused enough inflammatory reaction in the underlying choroid and retina to effect a firmer adherence to the sclera although there was very little if any histologic change to be seen. The eye itself tolerated the surgery well.

B. LAMELLAR SCLERAL RESECTION WITH DIATHERMY (THREE EYES)

Eye 4—enucleated at five days; no complications.
Eye 5—enucleated at one week; much vitreous lost.
Eye 6—enucleated at nine weeks; detailed description later.

There was evidence of somewhat more local reaction in Eyes 4 and 5 than in those in which diathermy was not used. The retina was recognizable as a layer but was entirely necrotic (fig. 2). There was much pigmentation of the choroid in the area of diathermy. The scleral reaction was not overwhelming but neutrophils and lymphocytes were present without epithelioids or giant cells; these appear about 10 days postoperatively. Again the retina was adherent in the surgical area and artefactually detached

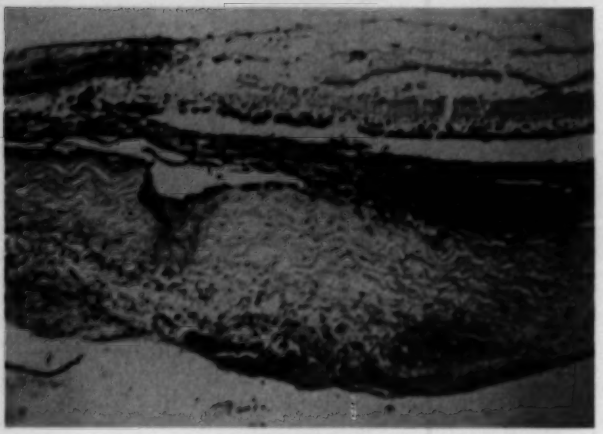

Fig. 2 (Asbury and Vaughan). *Eye 4.* Lamellar scleral resection with diathermy, enucleation five days postoperatively showing necrotic retina and pigment migration into choroid in the area of diathermy. (×30.)

elsewhere. The eyes in general had tolerated the procedure well and the vitreous seemed unaffected.

Eye 6 is worthy of more detailed analysis. A lamellar scleral resection with diathermy to the deep lamellar fibers was performed uneventfully and the postoperative course was uncomplicated. One week later under anesthesia the left eye of this monkey had been removed and an enucleation started on the right eye. Soon after the conjunctival incision was made there was a sudden loss of a large amount of formed vitreous which apparently escaped through the scleral wound. This was a result of direct pressure that was inadvertently applied to the globe by instrumentation. The eye was very soft and the enucleation was postponed so that the effect of this massive vitreous loss upon the function of the eye could be observed. The conjunctival wound was reapproximated and the lids sutured together with catgut. Amazingly, within three days the lid sutures had given way and the monkey was obviously able to see well (the other eye, it will be recalled, had been enucleated). The monkey was allowed to live for two more months and during this time had seemingly normal vision since he was in no way handicapped in his daily routine.

In sections of this eye (fig. 3), the adherence of the chorioretinal scar to the sclera was apparent and there was considerable pigmentation in the area. The inflammatory process had evidently quieted down, leaving some round cells, epithelioid cells, and a number of giant cells about the silk suture (fig. 4). The chorioretinal scar was apparently excellent in terms of retinal de-

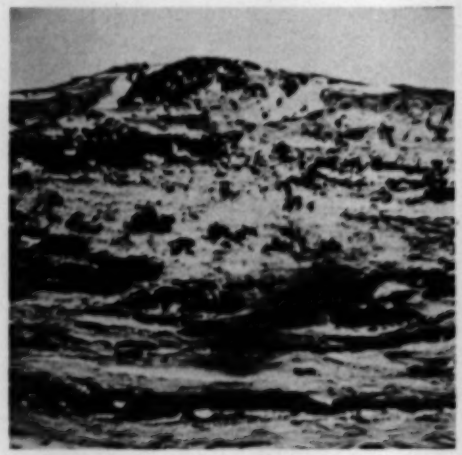

Fig. 3 (Asbury and Vaughan). *Eye 6.* Lamellar scleral resection with diathermy, enucleation nine weeks postoperatively showing chorioretinal-scleral scar and pigment migration into this area of diathermy. (×100.)

tachment surgery. The events also indicated that an eye is able to tolerate considerable vitreous loss and still retain normal function. There was surprisingly little histologic evidence of strands or condensations of vitreous.

C. FULL-THICKNESS SCLERAL RESECTION WITHOUT DIATHERMY (TWO EYES)

Eye 7—enucleated at two weeks.
Eye 8—enucleated at five weeks.

In Eye 7, a marked granulomatous response had occurred in the area of scleral resection two weeks postoperatively. Granulation tissue filled the scleral wound, and the typical foreign-body, granulomatous response, with lymphocytes, epithelioid cells, and foreign-body giant cells, could be seen around the silk sutures (fig. 5). The retina looked normal except in the surgical area where it was firmly anchored in the scleral-choroidal-retinal scar. In this scarred area the retina was unidentifiable. Elsewhere it had been artefactually detached (fig. 6). In some sections a few vitreous strands had formed and could be seen projecting a short way into the vitreous cavity. The reaction was much more marked than it was in eyes subjected to lamellar scleral resection, whether diathermy was used or not.

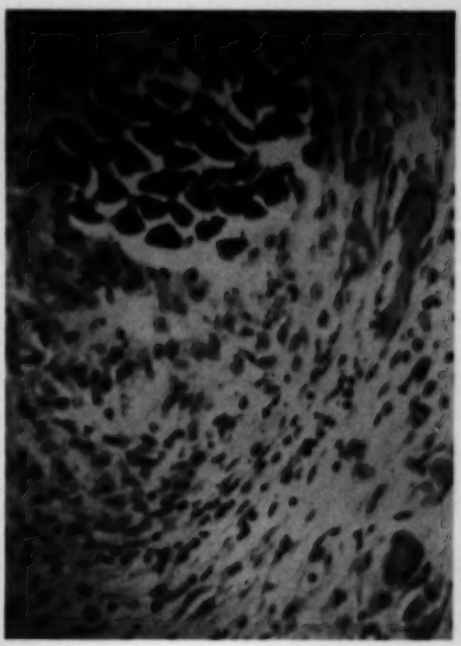

Fig. 5 (Asbury and Vaughan). *Eye 7.* Full-thickness scleral resection without diathermy, enucleation two weeks postoperatively, showing typical foreign-body, granulomatous response around silk suture. (×100.)

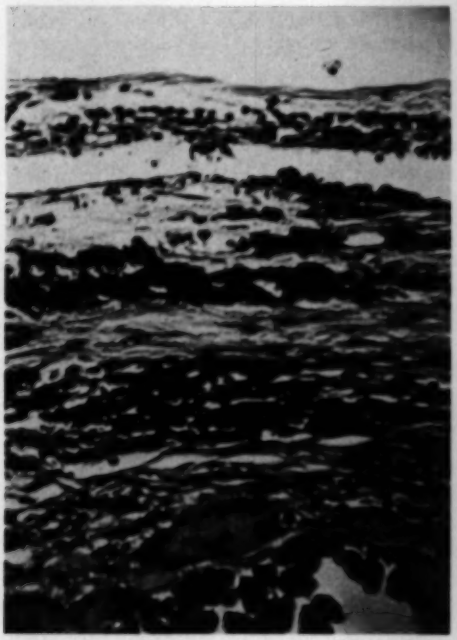

Fig. 4 (Asbury and Vaughan). *Eye 6.* Lamellar scleral resection with diathermy, enucleation nine weeks postoperatively showing low-grade inflammatory process still present. Note giant cells near the silk suture cut in cross section. The retina is quite necrotic but recognizable as a definite layer. (×100.)

In Eye 8, removed five weeks postoperatively, there was evidence of essentially the same response except that the reaction was further along, with scar tissue beginning to form. Both eyes tolerated surgery well and were functioning well at the time of death.

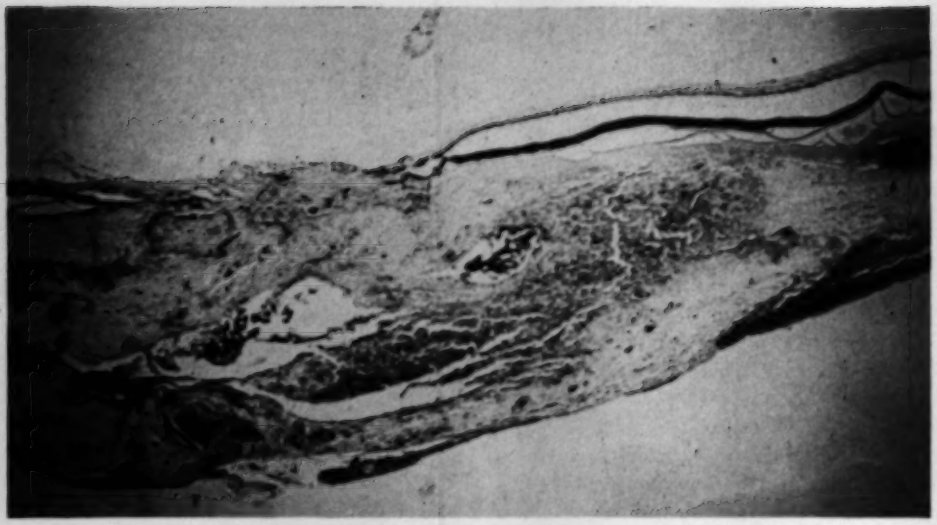

Fig. 6 (Asbury and Vaughan). *Eye 8.* Full-thickness scleral resection without diathermy, enucleation five weeks postoperatively, showing the retina artefactually detached except in the scleral-choroidal-retinal scar. (×18.)

D. MULTIPLE FULL-THICKNESS SCLERAL RESECTIONS (ONE EYE)

Eye 9—enucleated at two weeks.

The histologic appearance of this eye was very similar to Eye 7 already described (fig. 7). Again the marked granulomatous response could be seen in the area of the resection. The only noticeable difference was the reaction in the vitreous in which a number of definite strands had formed and were projecting outward and forward from the wound area toward the ciliary body (fig. 8). There was no vitreous loss or direct disturbance at the time of surgery so that this resection must have been secondary to the general scleral and choroidal reaction.

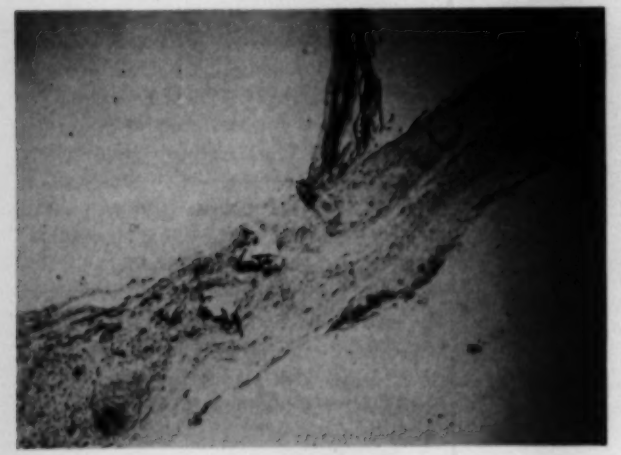

Fig. 7 (Asbury and Vaughan). *Eye 9.* Multiple full-thickness scleral resections without diathermy, enucleation two weeks postoperatively, showing normal artefactually detached retina dipping into scleral-choroidal-retinal scar and losing its identity. (×30.)

Fig. 8 (Asbury and Vaughan). *Eye 9.* Multiple full-thickness scleral resections without diathermy, enucleation two weeks postoperatively, showing vitreous strands projecting into the vitreous near point of insertion of normal retina. (×100. Same section as Figure 7.)

E. Scleral buckling without diathermy (two eyes)

Eye 10—enucleated at four weeks.
Eye 11—enucleated at six weeks.

The operations and postoperative courses were uncomplicated. A polyethylene tube the size of a No. 19-gauge Luer-Lok needle was used in Eye 10. This proved to be difficult to infold and in all other eyes a smaller tube, fitting a No. 25 needle, was used.

In general the sections of these eyes showed a moderate local scleral reaction with granulation tissue and a granulomatous re-

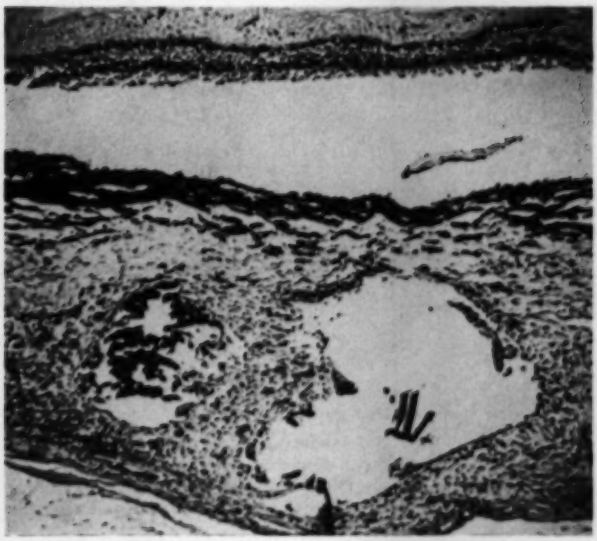

Fig. 9 (Asbury and Vaughan). *Eye 11.* Scleral buckling without diathermy, enucleation six weeks postoperatively, showing mild granulomatous response about silk sutures and polyethylene tube. (×60.)

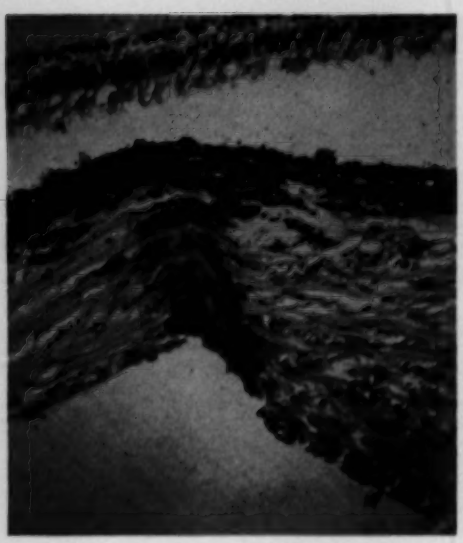

Fig. 10 (Asbury and Vaughan). *Eye 10.* Scleral buckling without diathermy, enucleation four weeks postoperatively, showing minimal reaction of lamellar scleral fibers and artefactual detachment of retina over the operative area. (×100.)

sponse about the silk sutures. There was also a mild granulomatous response in the area of the polyethylene tubing (fig. 9), although the inner lamellar scleral fibers seemed entirely normal with no infiltration of white cells (fig. 10). It was impossible to see the infolding in section as the eyes had become very soft and partially collapsed upon enucleation. For this relatively short period, the eyes had tolerated the tubing very well. The choroid and retina appeared entirely normal and less affected than by a lamellar scleral resection without diathermy as described above. The retinas of both eyes were detached artefactually, even over the operative areas (figs. 9 and 10).

F. Scleral buckling with diathermy (three eyes)

Eye 12—enucleated at one week.
Eye 13—enucleated at three weeks.
Eye 14—enucleated at four weeks.

These three operations were uneventful with no exposure of choroid or vitreous loss during the surgery. The postoperative courses were also uncomplicated. In sectioning Eye 12, which was removed one week postoperatively, it could be seen grossly (fig. 11) that the tube had nearly eroded into the vitreous cavity. Possibly a thinner than usual layer of scleral lamellae remained, or a stronger surface diathermy had been performed on the remaining fibers, but, whatever the cause, it could be seen histologically that a very thin, almost nonexistent layer was all that was keeping the tube from the vitreous cavity (fig. 12). The other two eyes did not show this tendency.

The reaction at one week was much more acute than at three or four weeks, with a predominance of neutrophils and no epithelioid or giant cells yet present. The choroid was lost in the scar in general, and the retina was necrotic with considerable migration of pigment epithelial cells into its substance (fig. 13). By three or four weeks the granulomatous response was apparent again and the retina could be identified as a definite layer with a few recognizable retinal cells, much fibrosis, and pigment migration (fig. 14). In Eyes 13 and 14 the retina was ad-

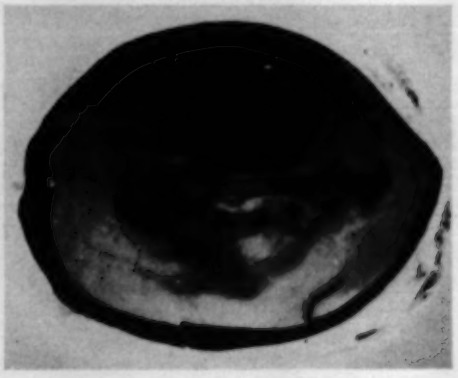

Fig. 11 (Asbury and Vaughan). *Eye 12.* Scleral buckling with diathermy, enucleation one week postoperatively, showing gross specimen from retinal side. The polyethylene tube has nearly eroded into the vitreous cavity.

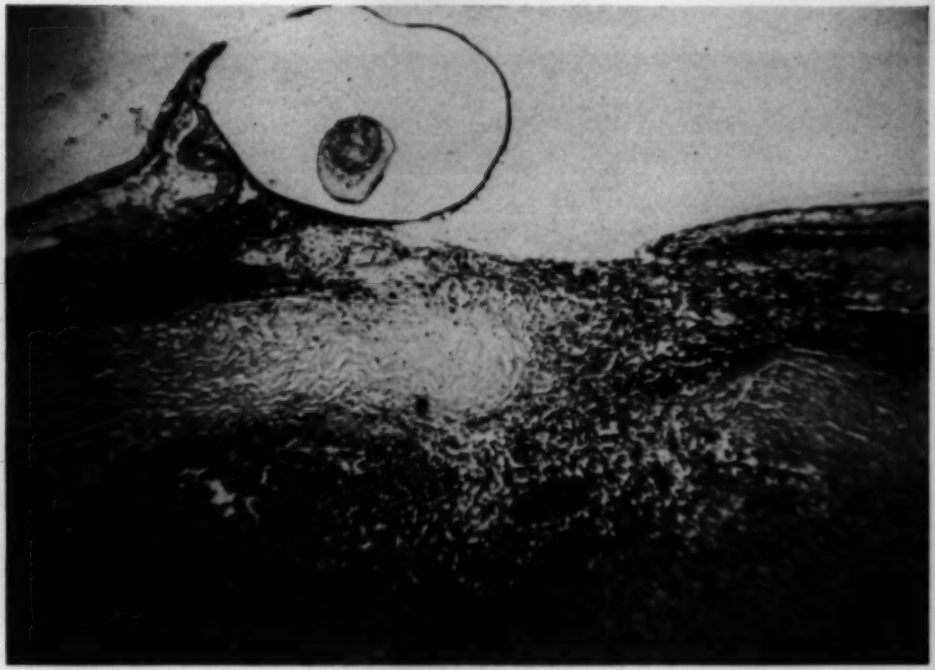

Fig. 12 (Asbury and Vaughan). *Eye 12.* Scleral buckling with diathermy, enucleation one week postoperatively, showing thin layer of tissue preventing polyethylene tube from projecting into the vitreous cavity. (×18.)

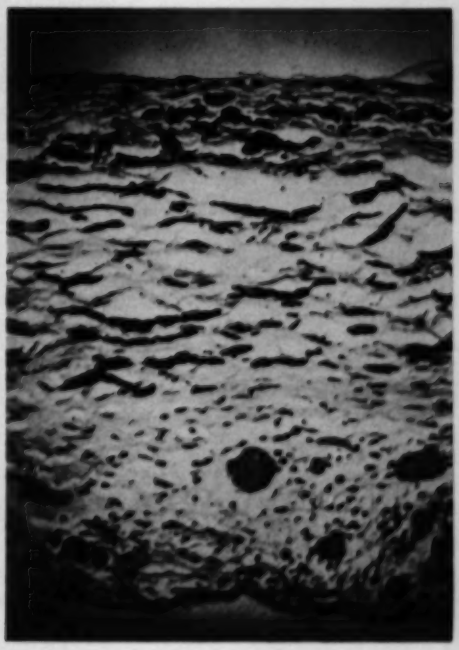

Fig. 13 (Asbury and Vaughan). *Eye 14.* Scleral buckling with diathermy, enucleation four weeks postoperatively, showing necrotic adherent retina with migration of pigment epithelial cells into its substance. (×100.)

Fig. 14 (Asbury and Vaughan). *Eye 14.* Scleral buckling with diathermy, enucleation four weeks post-operatively, showing necrotic adherent retina with pigment migration on the right side in area of diathermy, and relatively normal retina on the left side. (×100.)

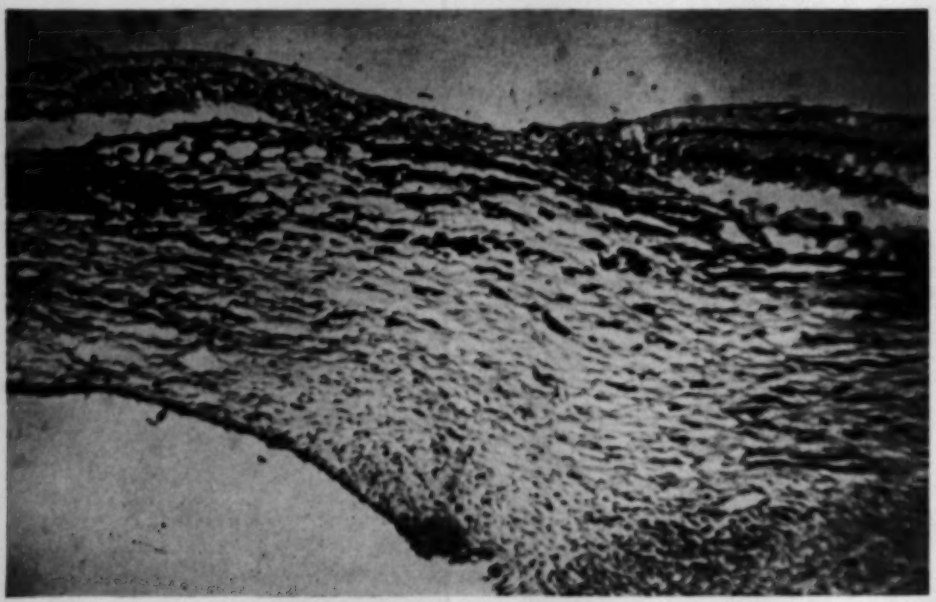

Fig. 15 (Asbury and Vaughan). *Eye 13.* Scleral buckling with diathermy, enucleation three weeks post-operatively, showing retina adherent to operative area and artefactually detached on both sides. (×30.)

Fig. 16 (Asbury and Vaughan). *Human eye.* Scleral buckling with diathermy, enucleation two weeks postoperatively, showing granulomatous response with round cells, epithelioid cells, and foreign-body giant cells. (×100.)

herent in the operative area and was artefactually detached nearly everywhere else (fig. 15). In none of the sections was vitreous change of any kind noted. All three eyes tolerated surgery very well and were functioning at the time of enucleation.

G. Scleral buckling with diathermy—human eye

The sections of this human eye are shown through the courtesy of Dr. John McGavic. A scleral buckling with diathermy of the lamellar fibers was performed two weeks prior to enucleation. The retina can be seen firmly attached at the operative site and only artefactually detached elsewhere. There is a marked granulomatous response with many lymphocytes, epithelioid cells, and giant cells, especially near suture remnants (fig. 16). The polyethylene tubing was lost in sectioning as it was in all the monkeys' eyes. The retina had undergone only the usual post-mortem change, even in the operative area (fig. 17). These pictures show histologically how similarly the human eye and the monkey eye respond to scleral surgery.

Discussion

As the animal whose sclera most nearly corresponds to human sclera, the monkey would seem to offer the best means we have for the experimental study of retinal detachment surgery. Moreover, the similarity of the histologic responses of the monkey and human eye to scleral surgery would seem to warrant the drawing of certain tentative conclusions which could have a

Fig. 17 (Asbury and Vaughan). *Human eye.* Scleral buckling with diathermy, enucleation two weeks postoperatively, showing retina that overlies operative area. The retina is normal except for postmortem changes, particularly of the ganglion-cell layer.

bearing on the techniques currently employed in retinal detachment surgery.

There can be no doubt that the full-thickness operation provokes much more reaction than the lamellar scleral resection. This has the obvious advantage of promoting a more adhesive chorioretinitis. On the other hand, if the reaction is violent enough to induce vitreous changes, including the formation of strands, then the stage may be set for future redetachment when these strands contract. In this connection it should be borne in mind, however, that the retinas of our monkey eyes had not been previously detached; in retinal detachment, the vitreous is protected by subretinal fluid and would presumably be less affected than it was in our experiments. There is no question, of course, as many authorities have pointed out, that lamellar scleral resection is much easier to perform and safer than the full-thickness operation.

With regard to diathermy, certainly none is required in the immediate area of full-thickness scleral resection since the reaction is already marked. It would seem to be rational, however, to apply mild surface diathermy to the deep lamellar fibers in performing lamellar scleral resection.

Multiple small scleral resections should be feasible when it is desirable to lessen the retinal pull in more than one direction. These should perhaps be lamellar since the one monkey eye (4), treated with three small full-thickness resections, showed marked vitreous changes although the vitreous was undisturbed during surgery. Silk sutures seemed relatively well tolerated although they did provoke a typical foreign-body type of granulomatous response.

Eye 13 demonstrated that an eye could sustain considerable posterior vitreous loss and still remain functionally useful. This would seem to support the opinion that vitreous loss is not necessarily a disaster in retinal detachment surgery.

It is even more difficult to draw conclusions about the scleral buckling operation on the basis of histologic interpretation. We have no opinion as to the permanency of the buckle. The results of monkey studies could hardly be applicable to the human eye in view of the difference in scleral thickness. The polyethylene tube is tolerated very well, up to four or six weeks at least, with a minimal foreign-body granulomatous response. In one eye in which diathermy was applied to the deep lamellar scleral fibers, it could be seen on section that the tube had nearly eroded into the vitreous cavity. This suggests that diathermy to the deep lamellar fibers, if applied at all, should be light when the polyethylene tube is to be used. It remains to be seen how human eyes tolerate polyethylene tubes over a long period of time.

It would appear that in some instances success in scleral surgery for retinal reattachment depends as much upon the cohesive chorioretinitis as upon the scleral shortening that is obtained. This is most likely to be the case when the scleral surgical site is near the retinal break. When one considers the amount of new granulation tissue that fills the scleral dehiscence caused by any type of scleral resection, one can account more easily for the long-term lack of permanent shortening that is so often reported as a clinical observation. Most observers feel that is not a disadvantage so long as the retina has a chance to become permanently attached since it is somewhat elastic and able to do the necessary stretching as the globe reassumes its original shape.

Although scleral buckling is clearly a more formidable procedure and causes more reaction than scleral resection, there is really no basis in this study for a comparison of the merits of the two operations. Indications for the use of one scleral operation, as superior to another under certain conditions, may in time evolve. For example, it would seem reasonable that in an eye with progressive degenerative myopia and multiple retinal

tears, a thin lamellar scleral resection plus diathermy would definitely be indicated, and that a large scleral buckle might offer the best hope for the cure of a long-standing detachment with fixed folds.

Full-thickness scleral resection has been advocated as the procedure of choice in the management of retinal cysts, the increased retinal and choroidal reaction helping to overcome the multicystic structure that is often so difficult to collapse effectively. At present each surgeon attains a certain percentage of cures with the consistent use of one, or at the most two, techniques.* Another surgeon, with an entirely different technique, attains a different percentage of cures but probably handles certain types of cases much better than others. In the future a thorough evaluation of the results of various methods may help establish criteria for the use of specific operations.

* It should perhaps be mentioned that well over half of all retinal detachment cases should of course be subjected to diathermy alone without scleral surgery of any kind.

Summary

1. Fourteen monkey eyes were subjected to scleral surgery of several types and were subsequently enucleated and examined histologically.

2. The operations performed were lamellar scleral resection (with and without diathermy), full-thickness scleral resection (single and multiple), and the scleral buckling operation of Schepens (with and without diathermy).

3. Some tentative conclusions were suggested by a comparison of the histologic reactions of these monkey eyes to the various types of surgery performed.

3549 Holly Lane.
220 Meridian Road.

We wish to thank Dr. Michael J. Hogan for his co-operation and helpful suggestions in carrying out this project.

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Ophthalmic Miniature

At supper the three Drs. of Physic again at my cabin, where I put Dr. Scarborough in mind of what I heard him say about the use of the eyes, which he owned, that children do, in every day's experience, look several ways with both their eyes, till custom teaches them otherwise. And that we do now see but with one eye, our eyes looking in parallel lines.

Diary of Samuel Pepys, May 24, 1660.

ON THE OPHTHALMOTONIC CONSENSUAL REACTION AND ITS RELATIONSHIP TO AQUEOUS HUMOR DYNAMICS*

EMILE L. PRIJOT,† M.D.
Liége, Belgium
AND
HOWARD H. STONE, M.D.
Baltimore, Maryland

It has long been known that a variety of manipulations of one eye would cause a change in intraocular pressure in the other eye. Magitot,[1] Morax and Girard,[2] and Larson[3] described a lowering of intraocular pressure in one eye after compression of the other eye. In 1924, Weekers[4] coined the phrase "ophthalmotonic consensual reaction" to describe this phenomenon.

As early as 1927, Wilmer[5] noted in experimental animals a fall in tension in one eye after a fistulization operation on the other eye. Since that time, similar findings were observed by Leplat[6] and Larson[7] after contusions; by Weekers[8] after cauterization of the sclera; by von Hofe[9] and others after subconjunctival injections; by Bonnefon[10] and others after intravitreous injection; by Nagata et al.[11] after puncture of the anterior chamber.

Davson and Quilliam,[12] working with nitrogen mustard and Evans blue, believed that severe lesions produced in one eye by local instillation of nitrogen-mustard potentiated the action of a mild nitrogen-mustard agent in the other eye in rabbits. They pointed out that often the permeability of the aqueous-blood barrier was increased in the contralateral eye after nitrogen-mustard was instilled in the other eye.

Linnen[13] studied the effect of a variety of trauma in one eye on the changes of intraocular pressure of the contralateral eye. On the basis of numerous experiments in rabbits he suggested that the "tonus" of the capillaries in the contralateral eye was changed by trauma in the other eye.

In these earlier experiments no methods were available for measurement of the rate of aqueous flow or the facility of outflow. More recently Bárány and Wirth,[14] working with rabbits which were subjected to intravenous infusion of para-amino-hippuric acid (PAHA), observed that in a few animals there appeared to be a complete, or almost complete, cessation of flow of aqueous humor in one eye after a paracentesis was performed on the contralateral eye. These authors suggested that, in addition to the possibility of consensual inhibition of aqueous flow, the flow could have been reduced in one or both eyes by the PAHA per se. Recent investigations by Linnér and Friedenwald[15] have shown that PAHA does reduce aqueous flow. The experiments of Bárány and Wirth with PAHA, therefore, do not prove that the apparent "consensual" inhibition of flow was solely a result of the paracentesis.

Becker[16] in experiments on rabbits severely compressed one eye while performing tonography on the other eye. He noted that during the one to two minutes of compression the tonogram on the other eye became flat, resuming its fall after the pressure was discontinued. The flat tonogram suggests that during this period both inflow and outflow ceased.

The purpose of the present study was threefold:

1. To re-examine the consensual ophthalmotonic reaction.

2. To explore some of the factors in-

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† Clinique Ophthalmologique, Université de Liége.

volved in the mechanism of this reaction.

3. To study pharmacologic agents which might alter the consensual ophthalmotonic reaction.

Methods and Materials

I. Experimental animals

A total of 73 rabbits were used in these experiments. The animals were pigmented male rabbits weighing between 2.2 and 3.0 kg.* They were fed a regular Sherwood-Feed pellet diet and water ad lib. Tonograms were obtained on rabbits by the methods described by Kornblueth and Linnér[17] and Stone and Prijot.[18] Three major types of experiments were carried out:

1. *Pentobarbital sodium anesthesia.* A group of rabbits was anesthetized by intravenous injection of pentobarbital sodium, U.S.P., 65 mg. per cc. in 10-percent alcohol using a dosage of 0.5 cc. per kg. body weight. Six minutes after the injection the intraocular pressure was determined tonometrically on one eye of each of the animals. This was repeated at intervals of five to 10 minutes up to 50 minutes from the beginning of the anesthesia. At the end of this period tonography was performed on the same eye (fig. 1). This procedure constituted the *control experiment.*

A week later the same procedure was repeated on the same eyes with one modification: at 20 minutes after the beginning of the anesthesia the other eye was compressed for four minutes (fig. 1). The compression was performed by means of a Bailliart ophthalmodynamometer adjusted to 40 gm. of pressure. This constituted the *compression experiment.* Henceforth, the eye on which tonometry and tonography is performed will be referred to as the *undisturbed* eye in contrast to the eye which is subjected to compression and which will be referred to as the *other* eye.

During the four minutes of compression the rabbit's head was held in its normal erect position, that is, not tilted to either side. This precaution was necessary to avoid any contra-coup pressure on the *undisturbed* eye. The dynamometer was held parallel with the surface of the table on which the animal was resting. The axis of the instrument made a 90-degree angle with the surface of the cornea on which it was applied.

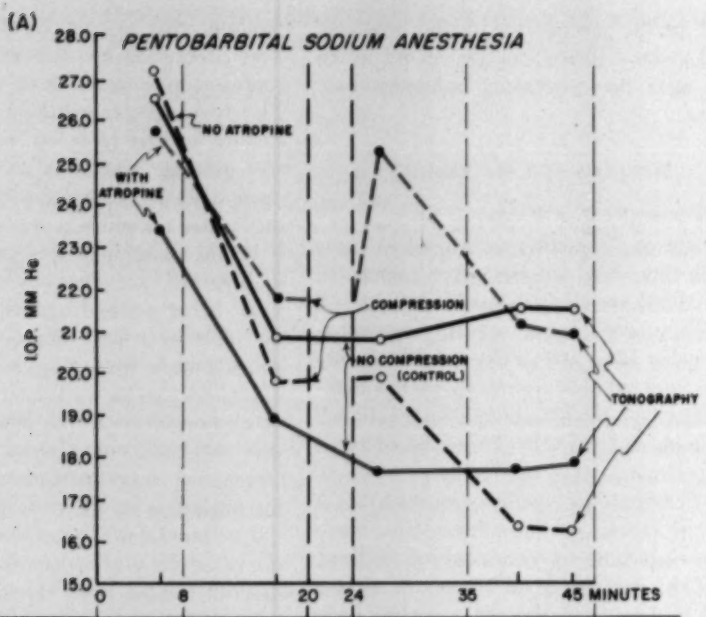
While tonography was performed on the *undisturbed* eye the other was protected from being pressed against the surface of the table by a soft ringtowel. Half of the animals were first subjected to the *control experiment* and a week later to the *compression experiment.* In the other half the order was reversed. One drop of 0.5-percent Ophthaine† was instilled into each eye at the beginning of the experiment.

2. *Paraldehyde anesthesia.* For reasons discussed fully elsewhere[18] the experiments described above were repeated under paraldehyde, U.S.P., anesthesia. A group of rabbits was anesthetized via gastric intubation using a dosage of 1.5 cc. paraldehyde per kg. body weight, mixed 1:7 with tap water. The first intraocular pressure determination on one eye was made 30 minutes after intubation and repeated at five- to 10-minute intervals up to 75 minutes. At 80 minutes tonography was performed on the same eye (fig. 2). One drop of 0.5-percent Ophthaine was instilled into each eye at the beginning of the experiment. Control and compression experiments were performed 10 to 12 days apart. In half the animals, the control, in the other half the compression, experiment was performed first.

3. *Atropine sulfate U.S.P.* A third group of rabbits received atropine sulfate by intravenous injection five minutes before the induction of general anesthesia (10 rabbits in this group had previously been used in experiments described above under (1) and (2). The dosage used was 30 mg. kg. body weight. The same type of experiments as described above were then performed on the atropinized rabbits. The period between *con-*

* E. R. Squibb & Sons, Co., New York.

† Purchased from Research Supply Co., Philadelphia.



(B)

MEAN RATIOS							
I.O.P. $\frac{\text{COMPRESSION}}{\text{NO COMPRESSION}}$ n=13	1.04±0.02	0.94±0.04	COMPRESSION	0.97±0.05	0.76±0.04 (*)	NO ATROPINE
I.O.P. $\frac{\text{COMPRESSION}}{\text{NO COMPRESSION}}$ n=10	1.11±0.04	1.17±0.08		1.46±0.13	1.22±0.11 (**)	WITH ATROPINE

(A) MEAN INTRA-OCULAR PRESSURES IN THE 'UNDISTURBED' EYE DURING A CONTROL PERIOD WITHOUT COMPRESSION (○——○), AND BEFORE & AFTER COMPRESSION (○— —○) OF THE OTHER EYE. WITHOUT ATROPINE (○——○) 13 RABBITS. WITH ATROPINE (●——●) 10 RABBITS.

(B) MEAN RATIOS & STANDARD ERROR OF THE MEANS OF I.O.P. $\frac{\text{COMPRESSION}}{\text{NO COMPRESSION}}$ IN THE SAME GROUP OF 'UNDISTURBED' EYES DURING THE TIME PERIODS INDICATED (MINS.)

(*) SIGNIFICANTLY LOWER THAN 1.00

(**) NOT SIGNIFICANTLY DIFFERENT FROM 1.00

Fig. 1 (Prijot and Stone). Results with pentobarbital sodium anesthesia.

trol and *compression* experiments was 10 to 12 days.

Since some rabbits are extremely insensitive to atropine because of an abundance of atropinase[19] only atropine-sensitive animals were used for these experiments. The rabbits were considered atropine sensitive if prolonged mydriasis was observed and a tachycardia of more than 250 beats per minute, after systemic atropine, was noted.

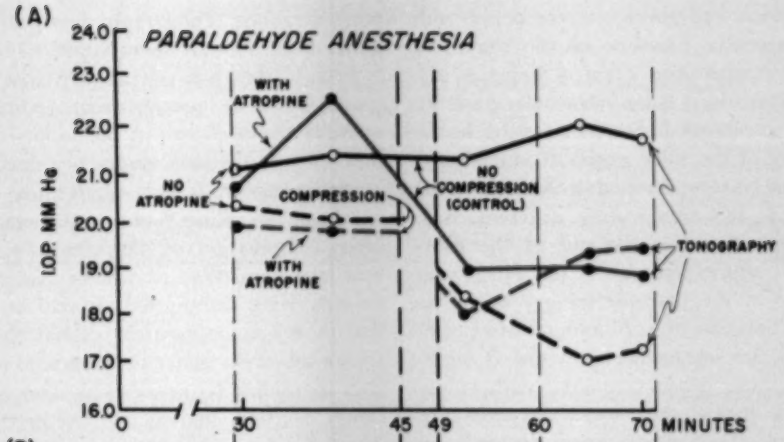
Episcleral venous pressure (P_v) before and after compression was obtained by the method described by Linnér.[21]

Flow (F) in rabbits was calculated according to the formula $F = C\ (P_o\text{-}9.0)$.

Ocular rigidity (K) was measured before and after compression. Determinations were made with the 5.5 gm. and 10.0 gm. weights. K was calculated from the tables of Friedenwald.[22]

II. Human subjects

Tonograms were obtained on seven healthy adult volunteers by the method of



(B)

MEAN RATIOS

I.O.P. COMPRESSION / NO COMPRESSION, n = 10	0.95 ± 0.06	COMPRESSION	0.86 ± 0.06	0.80 ± 0.05 (*)	NO ATROPINE
I.O.P. COMPRESSION / NO COMPRESSION, n = 10	0.90 ± 0.06		1.00 ± 0.12	1.10 ± 0.04	WITH ATROPINE

(A) MEAN INTRA-OCULAR PRESSURES IN THE 'UNDISTURBED' EYE DURING A CONTROL PERIOD WITHOUT COMPRESSION (○——○), AND BEFORE & AFTER COMPRESSION (○— —○) OF THE OTHER EYE. WITHOUT ATROPINE (○——○) 10 RABBITS. WITH ATROPINE (●——●) 10 RABBITS.

(B) MEAN RATIOS & STANDARD ERROR OF THE MEANS OF I.O.P. $\frac{\text{COMPRESSION}}{\text{NO COMPRESSION}}$ IN THE SAME GROUP OF 'UNDISTURBED' EYES DURING THE TIME PERIODS INDICATED (MINS).

(*) SIGNIFICANTLY LOWER THAN 1.00

Fig. 2 (Prijot and Stone). Results with paraldehyde anesthesia.

Grant.[20] Tonography was performed on the second eye of each individual two minutes after completion of tonography on the first eye.

Results

Figure 1 (Pentobarbital sodium anesthesia)

It will be seen from Figure 1 (A) that the intracular pressure falls in the first 15 minutes irrespective of whether or not the animals had received systemic atropine. It will also be seen that the intraocular pressure of the *undisturbed* eye during the *control experiments* (without compression) was essentially stable after 17 minutes (solid black line). In those animals which received atropine the pressure was stable after 25 minutes (solid red line.)

In contrast with the above *control experiments*, the intraocular pressure did fall in the *undisturbed* eye after four minutes of compression of the other eye in those animals which had not received atropine (interrupted black line). That this fall in intraocular pressure was statistically significant is shown in Figure 1 (B). The figures in the upper column labelled "no atropine" represent the mean ratios of intraocular pressure in the *undisturbed* eye during the

compression experiment as compared with the intraocular pressure of the same eye without compression *(control experiment)*. In other words, it is the intraocular pressure ratio of compression/no compression in the same eye of the same group of animals.

As can be seen, in the first 20 minutes the ratios are not significantly different from unity. Shortly after the end of the four-minute compression period the intraocular pressure in the *undisturbed* eye begins to fall and between 10 to 20 minutes after compression the intraocular pressure is significantly lower when compared with values obtained during the *control experiments*. The mean ratio compression/no compression was: 0.76 ± 0.04 ($p < 0.001$).

In the lower column *(with atropine)* of Figure 1 (B) the figures are given for another group of animals studied after intravenous atropine injections. Comparing again the values obtained after compression with those without compression, the intraocular pressure of the *undisturbed eye*, after compression of the other eye, was found to be somewhat higher than the control values (the mean ratio: 1.22 ± 0.11) though not significantly different. The sudden rise of intraocular pressure in the *undisturbed* eye after compression of the other in the atropinized rabbits was statistically significant (the mean ratio: 1.46 ± 0.13; $p < 0.01$). Tonography was performed as indicated on the graph during periods of steady-state conditions.

FIGURE 2 (PARALDEHYDE ANESTHESIA)

The results under this anesthetic were basically similar to those found under pentobarbital sodium anesthesia. After compression (interrupted black line) the intraocular pressure fell significantly in the *undisturbed* eye (the mean ratio: 0.80 ± 0.05; $p < 0.01$). Again this effect was not seen in atropinized rabbits (red lines). In contrast to the results obtained under pentobarbital sodium, there was no abrupt rise in tension in the *undisturbed* eye immediately after compression of the other eye in atropinized rabbits. Tonography was performed under conditions of steady-state.

From Table 1 it can be seen that under paraldehyde or pentobarbital sodium the mean of the coefficient of the facility of outflow (C) of the *undisturbed* eye during the *control* period was not significantly different from the values found in the same eyes after compression of the other eye. This was true regardless of whether or not the animals were atropinized. It will be noted that in the nonatropinized rabbits the C is somewhat larger under pentobarbital sodium than paraldehyde anesthesia. The significance of this finding is discussed elsewhere.[18]

In a control group of atropinized rabbits the C was determined without general anesthesia. These animals received only one drop of 0.5-percent Ophthaine instilled locally into the conjunctival sac. The mean values for C in this group was 0.27 ± 0.034.

Table 5 consists of a tabulation of values of intraocular pressure in human subjects at the beginning of tonography on each eye (P_o). In three subjects (J. B., H. S., and A. S.) tonography on each eye was repeated after a week's interval, this time performing the tonography first on the eye that previously had been *second*. At the right hand of the table the ratio of the intraocular pressure *second* eye/*first* eye is given for each pair of eyes. The mean of these ratios was 0.94 ± 0.02. This was significantly smaller than unity ($p = 0.02$). These results indicate then that after four minutes of tonography on one eye, the P_o in the second eye is lower than the P_o in the first eye.

COMMENT

The data presented were calculated on the assumption that the tables of tonometry, tonography, and ocular rigidity employed for human eyes may, in general, be applied to rabbit eyes with reasonable reliability. According to the work of Kornblueth and Linnér[17] such an assumption could be considered valid. Moreover, in comparing the tonographic determination on the same eye

TABLE 1

THE MEANS OF COEFFICIENT OF THE FACILITY OF OUTFLOW (C) UNDER GENERAL ANESTHESIA IN ATROPINIZED AND NONATROPINIZED RABBITS. C WAS DETERMINED IN THE UNDISTURBED EYE DURING A CONTROL PERIOD AND AGAIN AFTER COMPRESSION OF THE OTHER EYE

Anesthesia	No Atropine		With Atropine	
	Control (No compression)	After Compression	Control (No compression)	After Compression
Pentobarbital sodium	0.31 ± 0.02 n = 16	0.30 ± 0.02 n = 9	0.27 ± 0.02 n = 11	0.26 ± 0.02 n = 10
Paraldehyde	0.28 ± 0.01 n = 22	0.26 ± 0.02 n = 9	0.27 ± 0.01 n = 8	0.29 ± 0.02 n = 10

n = Number of rabbits in each group.

before and after a certain procedure was carried out, systematic errors tend to cancel out.

CONTROLS

There were several controls in the experiments described. First, all studies under general anesthesia were carried out twice: under pentobarital sodium and paraldehyde. Second, the same sets of eyes belonging to the same group of animals were used during the control experiments and the *compression* experiments. This was true of all groups of animals whether atropinized or not. Third, during the *compression* experiments the results obtained after compression were compared with the results before compression. Fourth, the results obtained during the *compression* experiments were compared with the results from the same eyes during the *control* (no compression) experiments. The results were expressed in terms of ratios compression/no compression (figs. 1 and 2) and these ratios, in turn, were analyzed statistically to ascertain whether or not they differed significantly from unity. Fifth, in the atropine group the same plan as has just been described was followed. Sixth, in the studies of ocular rigidity and episcleral venous pressure determinations were made on the *undisturbed* eye before and after compression of the other eye. Seventh, in all the series, half of the animals were first subjected to the *control* experiments and 10 to 12 days later to the *compression* experiments. In the other half the order was reversed.

INTRAOCULAR PRESSURE

It appears from Figures 1 and 2 that, in the nonatropinized rabbits the intraocular pressure in the *undisturbed* eye falls signi-

TABLE 2

MEAN AQUEOUS FLOW (F) MM.³/MIN. DETERMINED BY TONOGRAPHY IN THE SAME GROUPS OF RABBITS AS SHOWN IN TABLE 1

Anesthesia	No Atropine			With Atropine		
	No Compression (Control) (A)	After Compression (B)	B/A	No Compression (Control) (A)	After Compression (B)	B/A
Pentobarbital sodium	3.19 ± 0.27 *	2.19 ± 0.30 *	0.56	2.38 ± 0.32 Δ	3.20 ± 0.35 Δ	1.34
Paraldehyde	3.67 ± 0.25 ‡	2.11 ± 0.32 ‡	0.57	2.70 ± 0.24 #	3.02 ± 0.25 #	1.12

The calculation of the statistical significance of the differences between various pairs of (A) or (B) yielded the following results, 'p' being the probability that the differences could occur by chance:

‡ $p < 0.001$ Δ $p < 0.10$

* $p = 0.02$ # $p < 0.30$

ficantly after compression of the other eye. This decrease of intraocular pressure was not observed in atropinized rabbits. Under pentobarital sodium anesthesia it will be seen that a sudden rise of intraocular pressure in the *undisturbed* eye occurred shortly after compression of the other eye (fig. 1, interrupted red lines). This rise lasted only for about two to four minutes. It is not clear why this rise occurs and why it occurred under pentobarbital sodium and not under paraldehyde anesthesia. However, similar observations, under somewhat different conditions, were made on atropinized rabbits by Kahn and Loewenstein,[23] It seems probable that this sudden temporary rise in intraocular pressure is caused by a neurovascular reflex.

THE COEFFICIENT OF THE FACILITY OF OUTFLOW (C)

From Table 1 it appears that C does not change significantly in the *undisturbed* eye before and after compression. This was true whether or not the rabbits were atropinized. There appeared a slight trend toward a smaller C in the atropinized groups.

OCULAR RIGIDITY (K)

It can be seen from Table 3 that the ocular rigidity of the *undisturbed* eye was essentially the same before and after compression of the other eye.

EPISCLERAL VENOUS PRESSURE (P_v):

From Table 4 it appears that P_v of the *undisturbed* eye was not significantly different before and after compression of the other ($p < 0.2$). The small difference which was found could not account for the drop in intraocular pressure discussed above.

P_v in six atropinized rabbits, without general anesthesia, was found to be 9.0 ± 0.14 mm. Hg. This value is in good agreement with the findings of Seidel[24] in nonanesthetized rabbits and with value of Linnér[21] in anesthetized rabbits.

AQUEOUS FLOW (F)

The most striking feature of the data reported here was the finding with respect to aqueous flow. As can be seen from Table 2, in the nonatropinized rabbits, aqueous flow in the *undisturbed* eye after compression of the other eye was found to be reduced by approximately 40 percent. Flow was calculated from tonograms by the formula $F = C (P_o - P_v)$.

In the atropinized group of animals the picture appears somewhat more complicated. The scatter in the experimental data was greater in the presence than in the absence of atropine. Within the limits of uncertainty imposed by this scatter there was no significant difference between the rates of flow with or without compression of the other eye. Actually the rate of flow was greater after compression though not significantly greater. In any case atropine abolished the consensual inhibition of flow which occurred in the experiments without atropine. The immediate cause of the large experimental scatter in the atropine experiments was not clear but at the dosage levels used, the combination of atropine and general anesthesia

TABLE 3

MEAN RATIO OF OCULAR RIGIDITY (K) OBTAINED IN THE UNDISTURBED EYE BEFORE AND AFTER COMPRESSION OF THE OTHER EYE. THE FIGURE GIVES THE RATIO OF PAIRED MEASUREMENTS NOT THE ABSOLUTE VALUES OF MEASUREMENT

Ratio of 'K' $\frac{\text{Compression}}{\text{No Compression}}$
Mean = 1.13 ± 0.14
n = 11
$p < 0.40$

TABLE 4

EPISCLERAL VENOUS PRESSURE (P_v) IN THE UNDISTURBED EYE BEFORE AND AFTER COMPRESSION OF THE OTHER EYE

	Before Compression (Control)	After Compression
Episcleral venous Pressure (P_v) mm.Hg	9.75 ± 0.16	9.40 ± 0.16
	n = 6	n = 6

was close to tolerance limits. A considerable number of animals were lost after this combination of drugs. Those that died appeared to suffer from respiratory anoxia. It is possible that some of the survivors used in our experimental study were suffering from nearly fatal intoxication.

With respect to the findings in human eyes (table 5), it is worthy of emphasis that the *compression* which was caused by the tonometer over the four-minute period of tonography amounted to 16.5 gm. in contrast to 40 gm. which was used in the rabbits experiments. In the latter studies the period of four minutes was chosen purposely so as to be the same as that used in conventional clinical tonography; 40 gm. of constant compression was chosen as the most effective stimulus.

Preliminary experiments had shown that the intraocular pressure could be lowered in the *undisturbed* eye by (1) constant pressure over a period of four minutes with 16.5 gm. on the other eye, (2) puncture of the anterior chamber of the other eye, and (3) by the maintenance of marked hypertension in the other eye over a period of four minutes achieved by infusing isotonic saline into the anterior chamber under pressure.

None of these procedures, however, gave as consistent and as pronounced results as those with 40-gm. compression chosen in the previous experiments; 40 gm. of compression constituted, at least during the initial application, a considerable hypertension with respect to the eye on which it was applied.

From the foregoing it appears, then, that compression of one eye in rabbits is followed by a decrease in intraocular pressure in the other eye. This lowering of tension in the second eye is associated with a decrease in aqueous flow in that eye. This effect is not seen in atropinized rabbits, a fact which suggests the possible role of the parasympathetic nervous system in this reaction.

The data derived from the human eyes suggests the possibility that during conventional clinical tonography on the first eye the aqueous dynamics of the second eye might not be entirely in a steady-state condition by the time tonography is being performed on the second eye. Similar observations were made by Ballintine.[25]

TABLE 5

INTRAOCULAR PRESSURE (P_0) AT THE BEGINNING OF TONOGRAPHY IN SEVEN PAIRS OF NORMAL HUMAN EYES USING THE 5.5-GM. PLUNGER LOAD†

Initials	First Eye (A)	Second Eye (B)	Ratios B/A
J. B.	R.E. 13.4 mm Hg.	L.E. 12.8 mm Hg.	0.96
	*L.E. 13.1	R.E. 12.3	0.94
H. S.	L.E. 14.3	R.E. 14.0	0.98
	*R.E. 18.0	R.E. 14.0	0.78
A. S.	L.E. 15.0	R.E. 13.4	0.89
	*R.E. 14.0	L.E. 13.4	0.96
B. S.	15.6	15.3	0.98
J. M.	15.9	15.2	0.96
G. E.	14.2	14.3	1.00
W. B.	15.5	15.2	0.98
Mean	14.9±0.46	14.0±0.48	0.94±0.02 p=0.02

* Each second pair of determinations of P_0 were obtained one week after the first.

† Since the preparation of this manuscript, similar observations have been made on a total of 70 normal human subjects. Details will be published elsewhere.

Summary and Conclusions

The relationship between the consensual ophthalmotonic reaction and the dynamics of aqueous humor was studied in human and rabbit eyes. With respect to rabbits it was established that after compression of one eye the intraocular pressure in the other fell. This fall was found to be associated with a reduced flow of aqueous humor and with a normal coefficient of the facility of outflow, normal episcleral venous pressure, and a normal ocular rigidity.

No fall in intraocular pressure and no decrease in aqueous flow were observed if systemically atropinized rabbits were used. This finding suggests that the parasympathetic nervous system may participate in the consensual ophthalmotonic reaction.

Evidence has been presented to show that when clinical tonography is performed on a pair of human eyes, the second eye usually shows a lower initial intraocular pressure (P_o) than does the first eye.

University of Liége.

The Johns Hopkins Hospital (5).

Acknowledgment

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THE CLINICAL VALUE OF THE RODENSTOCK REFRACTOMETER*

FRANK I. HOBBS, M.D., AND ROBERT A. SCHIMEK, M.D.
Detroit, Michigan

The Rodenstock Refractometer is a recently developed aid for the busy refractionist. It has been advertised as permitting "objective determination of refractions" and "instantaneous readings of spherical and cylindrical refractions." This present study evaluates the performance and accuracy of the Rodenstock Refractometer on 242 patients (479 eyes) by comparing the Rodenstock determinations with customary manifest and cycloplegic refractions.

PRINCIPLES OF THE RODENSTOCK REFRACTOMETER

The basic principle of the Rodenstock Eye Refractometer is derived from the work of Schmidt-Rimpler[1] in 1866. His method for objective determination of the refraction of the eye incorporated a lens of known refractive power which was placed so that the secondary focal point coincided with the primary focal point of the eye under examination. In the present-day instrument, an illuminated test plate is positioned at the principal focus of a convex lens placed before the eye, so that parallel rays enter the eye. In emmetropia, these parallel rays come to a sharp focus on the retina. From this sharply focused retinal image, parallel rays emerge from the emmetropic eye and are focused by a convex lens in the manner of indirect ophthalmoscopy at the position of the test plate. In myopia the test plate must be moved closer to the convex lens to obtain a clear retinal image. In hypermetropia, the test plate must be moved farther away. Therefore, the position of the test plate which produces a clear retinal image measures the refractive status of the eye. More precisely, and in optical terms, the position of the test plate which produces a clear retinal image measures the far point of the eye in relation to the principal focus of the condensing lens.

COMPARATIVE ANALYSIS OF METHODS OF REFRACTION

In 242 patients (479 eyes) the Rodenstock determination was compared with the results of the usual manifest refraction and cycloplegic refraction. The distribution of the various refractive errors in this series is shown in Table 1. All of the Rodenstock Refractometer determinations were made without cycloplegic and were made by a trained technician* independently and in advance of the other methods of refraction. The manifest and cycloplegic refractions were subsequently performed by the ophthalmologist.† The final manifest refraction in each case was determined by noncycloplegic subjective trial with sphere and cross cylinder (usually starting with the noncycloplegic retinoscopy as an initial estimate). The value taken for the final cycloplegic refraction was that of cycloplegic retinoscopy modified by subjective cycloplegic methods (subjective trial with sphere and cross cylinder). No statistical comparison is made with pure retinoscopic values alone.

Comparisons are made between the Rodenstock determination and the final manifest refraction and between the Rodenstock determination and the final cycloplegic refraction. These comparisons are graphed as the Rodenstock error (or more correctly deviation) compared to the manifest or cyclo-

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* Mr. Alfred O. Johnson, Chief of the Optical Department, Henry Ford Hospital, kindly served as the Rodenstock technician during this study.

† The majority of the refractions were performed by one of us (R.A.S.). We are indebted to Dr. Harry W. Alcorn and other ophthalmologists in the clinic for some of the cases.

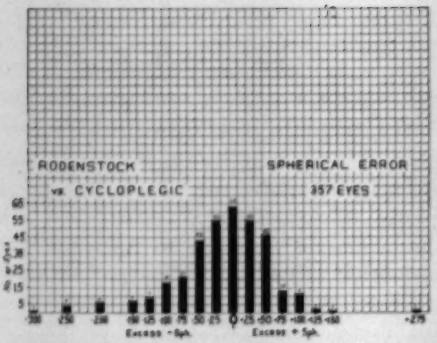
TABLE 1

SUMMARY OF REPORTED DATA

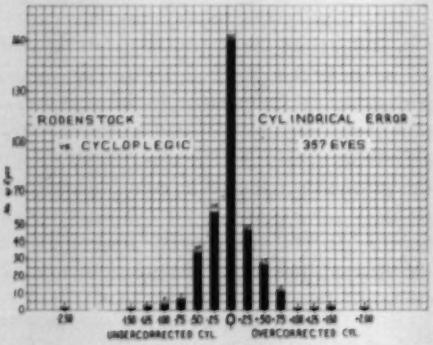
Total patients	242
Total eyes	479
Aphakic eyes	3
Emmetropic eyes	10
Myopic eyes	182
Hypermetropic eyes	284
Types of Refraction	
Rodenstock refractions (eyes)	479
Manifest refractions (eyes)	386
Cycloplegic refractions (eyes)	361
Eyes with all 3 methods	268
Rodenstock and manifest only	118
Rodenstock and cycloplegic only	93
	479

plegic determinations, since the latter two are the more accepted methods of refraction. These graphs show the distribution of differences between the individual Rodenstock reading and the manifest or cycloplegic refraction for all errors in sphere (graphs 1 and 5), cylinder strength (graphs 2 and 6), cylinder axis (graphs 3 and 7), and spherical equivalent (graphs 4 and 8). As can be seen, the results follow the standard deviation curve quite well. This is particularly true of the graphs showing the Rodenstock versus the cycloplegic determinations for all four error components (errors in sphere, cylinder strength and axis, and spherical equivalent). The average spherical error in this group is 0.48 diopters. The average cylindrical error is 0.31 diopters. The average axis error is 10 degrees.

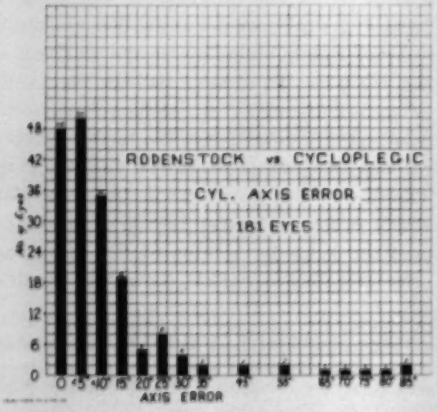
In the Rodenstock determinations versus the manifest refraction the average error was found to be slightly less in all components (sphere = 0.45 diopter; cylinder = 0.25 diopter; and axis error nine degrees). However, the curve is displaced from the standard deviation curve to an excess on the plus side in both the spherical correction and the spherical equivalent. In



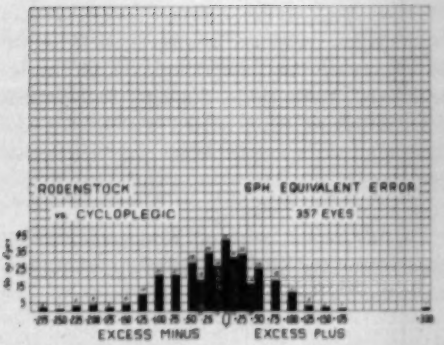
Graph 1 (Hobbs and Schimek). Rodenstock spherical error compared to cycloplegic conforming quite well to standard deviation curve. Shaded portions of this and subsequent graphs represent errors of 0.12 and 0.37D. and do not disturb contour of normal curve.



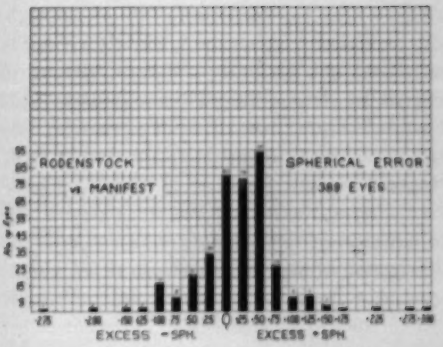
Graph 2 (Hobbs and Schimek). Good standard deviation curve of Rodenstock cylindrical error compared to cycloplegic refraction.



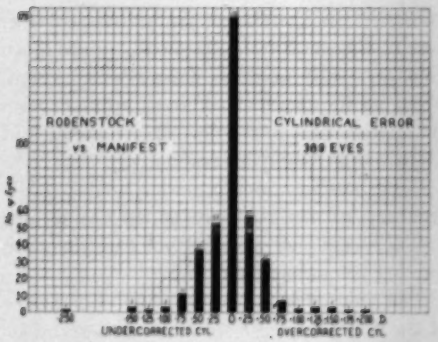
Graph 3 (Hobbs and Schimek). Rodenstock cylindrical axis error compared to cycloplegic determination conforming to standard deviation curve but showing a wide range of error.



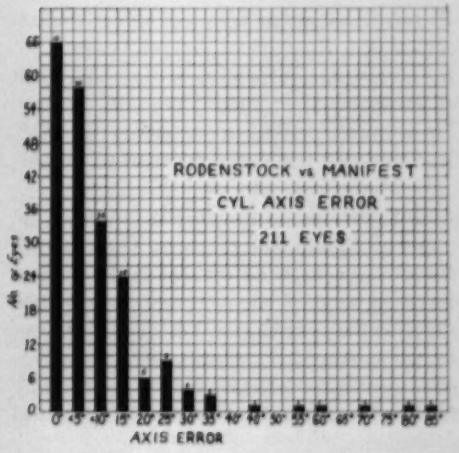
Graph 4 (Hobbs and Schimek). Good conformance of Rodenstock spherical equivalent error to standard deviation curve, compared to cycloplegic. Shaded portions represent errors of 0.12 and 0.37D. and do disturb normal contour of curve when added to next largest 0.25D. error.



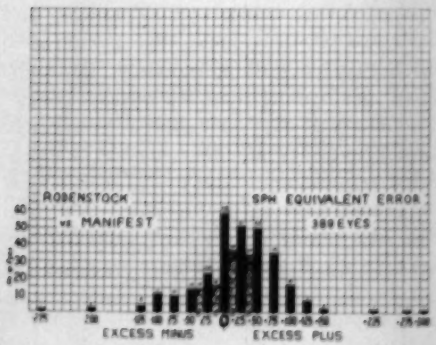
Graph 5 (Hobbs and Schimek). Rodenstock spherical error compared to manifest refraction showing a shift of the normal curve toward the plus side indicating less accommodative factor in favor of Rodenstock.



Graph 6 (Hobbs and Schimek). Rodenstock cylindrical error compared to manifest refraction conforming quite well to normal curve in distribution of error.



Graph 7 (Hobbs and Schimek). Cylindrical axis error of Rodenstock to manifest refraction conforming well to normal curve but showing occasional wide range of error.



Graph 8 (Hobbs and Schimek). Spherical equivalent error of Rodenstock to manifest showing considerable shift toward plus side, indicating less accommodation in favor of Rodenstock. Here again errors of 0.12 and 0.37D. disturb normal contour of curve when added to next largest 0.25D. error.

addition, the Rodenstock and the cycloplegic determinations agree more closely than the manifest and cycloplegic determinations in regard to their spherical equivalents. This would indicate that there tends to be less accommodative factor in the noncycloplegic Rodenstock determination than in the usual manifest refraction, if properly performed by an experienced operator. The cylindrical determination in the manifest study corresponds quite closely to that of the cycloplegic study. Individual Rodenstock determinations were equally accurate for either myopic or hyperopic eyes according to statistical analysis. For either a myopic or a hyperopic error, similar deviation curves were obtained showing the Rodenstock error as compared with the manifest or cycloplegic refraction. Therefore, it may be concluded that the type of refractive error does not effect the accuracy of a Rodenstock determination.

The average refraction is not carried out to an accuracy of more than 0.25 diopter. Thus in our calculations, errors of 0.12, 0.37, and so forth, were represented graphically as the next largest 0.25 diopter. The shaded portions on the graphs represent errors of 0.12 and 0.37 diopters. These do not disturb the contour of the standard deviation curve in any of the determinations when added to the next largest 0.25 diopter, except for some irregularity of the spherical equivalent curve. This is to be expected, since many fractions occur on calculation of spherical equivalents.

Discussion

General observations on the Rodenstock Refractometer during this study may be compared with those mentioned in a previous study by Bradford and Lawson.[2] They found good correlation between the cycloplegic Rodenstock determinations and both the cycloplegic retinoscopy and the subjective cycloplegic refractions (0.23 to 0.26 diopters of spherical error and 0.38 to 0.43 diopters of cylinder error with less than five degrees axis error). Their noncycloplegic Rodenstock determinations varied more widely from the subjective cycloplegic refractions. Their noncycloplegic Rodenstock determinations also varied more than the dynamic retinoscopy from the subjective cycloplegic refractions, particularly in reference to spherical finding.

In this series, with all Rodenstock readings performed by one technician, we did not find the accommodative factor to be as troublesome as was the case in the series of Bradford and Lawson. If anything, less accommodative factor was found than in the manifest refraction. It should be emphasized that all of the Rodenstock readings were done by one individual and that facility in taking a rapid reading and getting the patient to relax his accommodation will greatly influence the results as far as accommodation is concerned. Contrariwise, much more difficulty with accommodation was experienced by the resident and staff ophthalmologists when first using the refractometer and when using it only occasionally.

Early studies on this series analyzed the accuracy of the Rodenstock determinations for different age groups, but the variation was not felt to be significant.

The chief disadvantage in the clinical use of the noncycloplegic Rodenstock determination is that a considerable degree of technical proficiency is necessary to obtain an accurate and therefore useful result. All of the ophthalmologists in our clinic preferred retinoscopy to the Rodenstock instrument. Their impression that retinoscopy was quicker and easier was probably due to their greater skill and familiarity with retinoscopy. The technician performing the Rodenstock determinations was also an expert retinoscopist. With proficiency at either method, he preferred retinoscopy to use of the Rodenstock for general ease of performance. Although these are merely impressions, they indicate that accurate Rodenstock determinations are not usually as "instantaneous" and simple as we might be led to believe.

The second disadvantage is the occasional wide variation from the usual methods of refraction. With care and experience, this is probably no greater a deviation from the usual refraction than is experienced with noncycloplegic retinoscopy. The apparent variability of the instrument in the hands of beginners can be an annoying and disappointing feature.

A third limitation is that this method cannot be used on eyes with cloudy media, corneal opacities, or cataracts.

It is generally agreed with Bradford and Lawson that the use of the Rodenstock Refractometer is not unreasonably difficult or time consuming, and gives a reasonable approximation of the refractive status of the eye, even without the use of cycloplegia. With a technician using the Rodenstock instrument before the customary manifest refraction, the Rodenstock determination can save some time.

Summary

Rodenstock Refractometer refractions under noncycloplegic conditions are compared to cycloplegic and manifest refractions in 242 patients. The results are graphed and show close conformation with the standard deviation curve. The noncycloplegic Rodenstock reading usually closely approximated the manifest and cycloplegic refractions, and tended to show less error due to accommodation than the average manifest refraction in our series. The Rodenstock Refractometer appeared equally accurate for all of the various refractive states and for all of the various age groups of patients old enough to co-operate. This indicates that the Rodenstock Refractometer can have a place in the armamentarium of the busy ophthalmologist who has a technical assistant to perform the readings, despite occasional large errors of deviation.

Henry Ford Hospital (2).

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CYCLOGONIOTOMY*

A new operation for chronic glaucoma: a preliminary report

Otto Barkan, M.D.
San Francisco, California

The principle of operating in the chamber angle with visualization by means of a gonioscopic contact glass was introduced by me in 1936[1] (goniotomy). The objective of the operation was to incise the obstructed trabecula thereby restoring outflow from the anterior chamber to the Schlemm's canal system.

Goniotomy proved successful in congenital glaucoma in a high percentage of cases[2-7] (over 80 percent). However, in adult chronic simple (wide- or open-angle) glaucoma, the good results were not sufficiently consistent to recommend its use.

I, therefore, developed a technique of goniotomy in which, after deepening of the anterior chamber, an incision at the root of the iris, posterior to the scleral spur, separates the ciliary body from its attachment and creates a communication between anterior chamber and suprachoroidal space.

* Presented at the 53rd annual meeting of the Ophthalmological Society of Egypt, Cairo, March 16, 1956.

Since this form of goniotomy consists of an incision and separation of the tendinous insertion of the ciliary muscle and ciliary body, I have called it "cyclogoniotomy." As a result of visualization and deepening of the anterior chamber, the formation of the cleft can be precisely controlled.

The objective of forming a cleft into the suprachoroidal space is similar to that of cyclodialysis and its variants. However, cyclogoniotomy, because of its approach across the anterior chamber and because of direct magnified vision, is a different operation—there is no disturbance of vision and almost no traumatism. Since the incised area is avascular, the incision is without hemorrhage. It produces superior results with safety and without early or late complications.

Indications

Cyclogoniotomy has been used with excellent results in a total of 23 cases. Seventeen were cases of primary (wide- or open-angle) glaucoma, of which five were operated upon from two to three years ago. In one patient the pressure was normalized for three years until her decease. In two the pressure has remained normalized for three years and in two for two years until the present time. In 12 patients the periods of observation have been from nine to 12 months, and in two for four months.

One case of primary narrow-angle glaucoma (angle-closure or closed-angle), in which the angle was closed by adhesions and iridectomy had failed, has been normalized, up to the present time, for a period of 12 months.

One case of aphakia in which the trabecula was obstructed, and two cases out of seven of advanced distended congenital glaucoma in which goniotomy (trabeculotomy) and several other operations had failed, have been normalized over a period of 12 months.

The procedure would appear to be indicated also in juvenile glaucoma (congenital glaucoma of delayed onset and premature simple glaucoma) but no case of this type has as yet come to operation.

Technique

In adult simple (open-angle) glaucoma the technique is as follows:

The usual preoperative sedation and antibiotic medication for intraocular operation is given. Maximal miosis is obtained by the instillation of an extra drop of prostigmine (five percent) three times, at half-hour intervals before operation.

Anesthesia may be local combined with intravenous demoral, or general (sodium pentothal intravenously). The face is prepared and the eye irrigated in the usual manner. A face mask of dark color is used to prevent glare.

Akinesis is performed. Partial canthotomy is required for maneuverability of the contact glass. Four drops of ophthaine (one percent) are instilled at intervals of one minute. The eye is kept closed in order to maintain the luster and transparency of the epithelium. Care must be taken to prevent the anesthetic drops from clouding the corneal epithelium. Since perfect visibility is essential for this procedure, any quantity or prolongation of anesthetic which clouds the epithelium must be avoided. When the fourth drop of ophthaine has been instilled, a retrobulbar injection of two or three cc. of a solution of two parts of physiologic saline and one part of Xylocaine (two percent) is made to help immobilize the eye. The ensuing steps of the operation proceed immediately.

Fixation. While the eye is rotated down by an assistant with a mouse-tooth (Bishop-Harmon) forceps applied at the limbus at the 6-o'clock position, the superior rectus is grasped with Gifford forceps with spring lock. The fixation of the tendon of the inferior rectus is similarly performed.

Deepening of the anterior chamber. Deepening is performed as the first step. It may also be performed simultaneously by continuous injection with an anterior chamber

puncture needle or by means of a combined chamber puncture needle and goniotomy knife.* In the following the deepening as the first step is described.

With an anterior chamber puncture needle (Amsler) an oblique self-sealing corneal puncture is made one mm. from the corneoscleral border, at the 7-o'clock position when the operation is performed on the right eye and at the 5-o'clock position on the left eye. The needle is attached to a two-cc. Luer syringe which is one-third filled with physiologic solution of sodium chloride. The solution is injected until the iris lens diaphragm is pushed well back, but avoiding excess pressure. This affords ample space for the knife to cross the chamber. (The increased pressure in the anterior chamber prevents the iris from falling before the knife during the making of the cleft.)

The room is in semidarkness. For illumination a nurse holds an air-cooled plastic hammer lamp[8] in contact with the right temple of the surgeon. Transscleral illumination at the limbus with a focal illuminator[9] can be helpful. It is advisable for a presbyopic surgeon to wear a correction for a distance of seven inches in addition to a telescopic loupe. The surgeon stands at the patient's side with the eye at about waist level.

Before application of the surgical contact glass, the head is rotated to the contralateral side and the eye adducted. This prevents ingress of air under the glass. The surgical contact glass† (medium size) is applied in the usual manner by injecting physiologic saline solution between it and the cornea through a curved cannula and a two-cc. Luer syringe. The surgeon controls the glass with the left index finger. The eye is then abducted slightly in order that there may be ample room to push the glass nasally. A temporal crescent of the cornea, two to three mm. wide where the puncture is to be made, is exposed.

The puncture is made with a goniotomy knife,* one mm. axial to the corneoscleral border and a little obliquely so that the corneal wound is valvelike and self-sealing. It must not be too oblique lest it impede the passage of the tapered shaft as it crosses the chamber. The anterior chamber is never lost if a correctly tapered knife is used, and it is not retracted during the operation.

The initial position of the surgeon is such that he sees the blade through the glass as it enters the chamber. Lowering his position he then guides it into the angle. The blade is inserted at the apparent attachment of the iris and to a depth of one mm. which is equal to the length of the blade. The incision is made counter-clockwise. The iris falls back forming a cleft or cavern which leads into the suprachoroidal space. The deepening of the chamber stretches the iris back, encouraging the cleft to gape.

The separation of the ciliary body from its attachment is under direct visualization. The cleft should cover one sixth of the circumference. When it has been completed, the knife is quickly removed, while pressure is exerted against the back of the blade in order to prevent enlargement of the puncture wound of the cornea. Contact glass and fixation forceps are removed. Some aqeous loss is induced lest the increased pressure in the anterior chamber resulting from the injection of saline solution encourage closure of the cleft.

In primary simple (open-angle) glaucoma, since the incision is in avascular tissue far removed from the anterior ciliary vessels and since the iris and sclera are not touched, there is no hemorrhage.

The head is rolled onto the operated side and one-third of the anterior chamber is filled with air injected through the puncture wound by means of a curved cannula and a two-cc. Luer syringe. If the head is rotated so that the air bubble rises into the operative

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* The cannulated needle-knife which has been devised for this purpose can be obtained from Ernst Griesshaber, Schaffhausen, Switzerland.

† Parsons Optical Laboratories, 518 Powell Street, San Francisco.

site, the raw surfaces of the angle are kept apart and the air is locked in the chamber. The miotic pupil must not be occluded by the air bubble lest pupillary block and air glaucoma develop.

The speculum is removed and the canthotomy closed with catgut. Antibiotic and cortisone ointment is inserted into the conjunctival sac and the eye is covered with a pad and metal shield.

The success of gonioscopic surgery depends upon attention to detail. Perfect visibility through a completely clear cornea and contact glass is essential. If due to delay or for any other reason visibility is disturbed, the operation should be deferred to another day.

Postoperative care

The patient is kept in bed on the operated side for one day so that the injected air will keep the raw surfaces of the operated region apart and not block the pupil.

The pupil usually remains moderately contracted (two mm.) and retains its reaction to light. After the first day hydrocortisone drops (0.5 percent) are instilled three or four times a day to prevent irritation. Postoperatively, miotics are at first avoided unless the pupil tends to dilate over two mm. Mydriatics are contraindicated because they would encourage closure of the cleft. They are not required because pupillary adhesions are not likely to form, the iris not being irritable and the pupillary reaction to light being preserved.

Patients are hospitalized from two to three days and then observed ambulatory.

After one or two weeks, one drop of a miotic (prostigmine or pilocarpine, one percent) is instilled at least once daily (before retiring) to ensure the cleft remaining open.

Summary

Cyclogoniotomy is performed in the chamber angle, under gonioscopic control, with visualization by means of a contact glass. It reduces the pressure by forming a communication between anterior chamber and suprachoroidal space.

Cyclogoniotomy has advantages for the surgical treatment of both early and late, chronic simple (wide- or open-angle) glaucoma, and certain other forms, in that it is atraumatic and safe. It is free of hemorrhage, postoperative adhesions, disturbance of vision, or other early or late complications.

Excellent results have been obtained in 23 cases over periods extending from four months to three years. Longer periods of observation will further determine the permanent effect of the operation. This report is published in order to encourage a more extensive trial of the procedure.

490 Post Street (2).

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THE PRODUCTION OF ANAPHYLAXIS*

IN GUINEA PIGS WITH HETEROLOGOUS UVEAL TISSUE

TED SUIE, PH.D., AND FRANK W. TAYLOR, M.D.
Columbus, Ohio

INTRODUCTION

In 1910, Elschnig[1] elicited anaphylaxis in guinea pigs by sensitizing and subsequently shocking them with rabbit uveal suspension. Woods,[2] who has reviewed exhaustively the literature on this subject, noted that many investigators since then have confirmed the fact that uveal tissue is antigenic as evidenced by various immunologic manifestations. Others have not been able to support these findings.

Collins[3] found that a certain percentage of guinea pigs which were inoculated with homologous uveal tissue incorporated in Freund's adjuvant (intramuscularly and intraperitoneally) developed histopathologic changes in the choroid. In a later communication[4] the same author found that animals given cortisone during and following the injections demonstrated a more marked choroidal reaction than the nontreated group. Recently, Naquin[5] attempted to produce hypersensitivity to homologous uveal tissue combined with Freund's adjuvant in guinea pigs by subcutaneous injections. He was unable to (1) detect histologically a positive uveal pigment skin test, (2) demonstrate a tuberculin-type reactivity to uveal tissue, (3) find changes in the eyes of these animals.

In a previous paper,[6] one of us (Suie) reported that rabbits which were sensitized intraocularly and subsequently inoculated intravenously with homologous uveal tissue developed inflammatory reactions in the anterior chamber of the sensitized eyes. However, animals which were inoculated into the footpads with uveal suspension and Freud's adjuvant did not demonstrate an ocular response. In both groups complement-fixing antibodies could be demonstrated.

The state of anaphylaxis which has been shown unequivocally to be concerned with a specific antibody-antigen reaction is considered to be one of the most sensitive in vivo tests for determining antigenic potentials of various substances. Therefore, in view of the conflicting evidence concerning the antigenicity of uveal tissue, this investigation was an attempt, first, to confirm Elschnig's original findings and, secondly, to determine the effect of cortisone on such an immunologic phenomenon, if it does exist.

METHODS AND MATERIALS

Normal guinea pigs of both sexes and weighing between 400 to 475 gm. were used throughout these experiments. Both albino and pigmented animals were used.

The uveal tracts were removed from eyes of freshly killed beef cattle by the following procedure:

The eyes were immersed in 1:1,000 Zephiran for 15 minutes. The cornea was incised widely with a Bard-Parker No. 15 blade. The lens was extruded by pressure on the posterior pole of the eye. The iris and ciliary body were removed by grasping the iris with a tissue forceps and by gentle traction causing a separation at the pectinate ligament. Continued gentle traction then resulted in the delivery of the iris and ciliary body intact. The retina remained behind though frequently became detached. Strict aseptic technique was used. The sterility of the uveal tracts which had been washed copiously in sterile saline was verified in thioglycollate broth without indicator. The tissues which had been previously weighed were ground in an ultrahomogenizer at approximately 45,000 rpm. Enough sterile normal saline was added to make a final dilu-

* From the Department of Ophthalmology, College of Medicine, The Ohio State University.

tion of 1:40. This concentration of homogenate was used for both the sensitizing and shock doses.

Group I consisted of 20 guinea pigs which were sensitized intraperitoneally with 0.5 ml. of uveal suspension and intramuscularly with the same amount. Thereafter, at three-day intervals for a total of nine days, 1.0 ml. of this material was injected intraperitoneally. Seven to 10 days later the animals were challenged with 4.0 ml of the uveal homogenate directly into the heart. (The amount given as the shock dose was predetermined by previous titrations with various quantities. It was found that 3.0 to 4.0 ml. of the suspension was adequate for intoxication of sensitized animals.) The animals were observed carefully for signs of anaphylaxis.

Group II consisted of 18 guinea pigs which were sensitized in the same manner as those described above. Twenty-four hours and one hour prior to the shock dose these animals were given a total of 50 mg. of cortisone acetate intramuscularly (25 mg. per injection).

Group III (controls) consisted of six animals which had not been sensitized but were shocked intracardially with 4.0 or 5.0 ml. of uveal suspension.

Findings

Table 1 indicates the number of guinea pigs demonstrating anaphylaxis. Approximately the same percentage of animals displayed some degree of anaphylaxis in Groups I and II (90 percent and 83 percent). However, more deaths occurred in the cortisone-treated group. The controls which were not sensitized but shocked showed no anaphylaxis. They were observed for a period of three months.

Guinea pigs which responded severely to the shock dose of antigen exhibited all the classic signs of anaphylaxis. These consisted of irritability, several characteristic coughs, voiding of feces and urine, dyspnea, convulsions, and finally death. Death in the majority of cases occurred within a few minutes after the shock dose was administered. Animals which were autopsied immediately after death demonstrated fibrillations of the heart, marked floatability of the lungs in water, and hemorrhagic areas in the viscera. All of these signs are associated with fatal anaphylaxis in the guinea pigs.[7] Those animals showing a lesser degree of sensitivity demonstrated all the above signs except convulsions and death. Characteristically, these animals gradually recovered soon after the shock dose in spite of very severe symptoms. Several of the guinea pigs reacted only mildly to the shock dose of uveal homogenate.

Discussion

Because of conflicting reports in the past, this investigation was instigated to determine

TABLE 1

THE EFFECT OF SENSITIZATION AND SHOCK WITH HETEROLOGOUS UVEAL TISSUE

	Number of Guinea Pigs	Anaphylaxis		Anaphylaxis Not Demonstrated
Group I	20	Died	6	2
		Survived	12	
		TOTAL	18	
Group II (Cortisone terated)	18	Died	10	3
		Survived	5	
		TOTAL	15	
Group III (Nonsensitized)	6		0	6

whether uveal tissue is antigenic. The anaphylactic approach was chosen, since most investigators will agree that this method is one of the most sensitive in vivo tests for determining the antigenicity of various substances. Classic anaphylaxis was produced in the majority of guinea pigs.

Attempts to block the shock with cortisone failed. This finding is in agreement with most investigators who have found that cortisone seemingly has no apparent effect on experimental anaphylactic shock in guinea pigs or in vitro response of smooth muscles to homologous sensitizing antigen. Thus, Landau[8] et al. found that ACTH and cortisone did not prevent anaphylactic reactions in vivo and in vitro in actively or passively sheep-serum sensitized guinea pigs. They concluded that "in the guinea pig administration of ACTH or of cortisone in the doses used does not prevent the union of antigen and antibody, nor interfere with the effects of such union, nor does it protect against histamine reactions." Leger and his co-workers[9] and Friedlaender and Friedlaender[10] reported similar results.

Summary

1. Anaphylaxis was produced in guinea pigs by sensitization and subsequent shocking with bovine uveal homogenate.

2. In the concentrations used in this study, cortisone did not inhibit the anaphylactic response in guinea pigs.

3. This study would indicate that uveal tissue is antigenic for guinea pigs.

The Health Center (10).

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THE INHIBITORY EFFECT OF AQUEOUS HUMOR ON THE GROWTH OF CELLS IN TISSUE CULTURES*

WALTER KORNBLUETH, M.D., AND ESTHER TENENBAUM, PH.D.
Jerusalem, Israel

The clinical observation that aseptic wounds of the iris do not form scar tissue has never been satisfactorily explained. A surgical coloboma of the iris remains unaltered during life and an iridodialysis leading even to aniridia is not followed by proliferation of connective tissue as long as no inflammation accompanies the injury. However, following irritation, the iris is capable of forming granulation and scar tissue in profusion.

There are few histologic studies of iridectomies in man. Henderson[1] stressed that years after iridectomy the iris appears exactly as it was immediately after the operation. The iris tissue forming the pillar of the coloboma remains raw and unhealed and exposed to the aqueous humor. There is no tendency for either endothelium or epithelium to cover the defect. McBurney[2] noted the scanty nature of the exudate in the iris four days following iridectomy. About the iris stump he found only a small amount of fibrin and a moderate number of polymorphonuclear leukocytes and lymphocytes. A more marked cellular infiltration appeared in the uninjured portion of the iris.

The only experimental approach to the healing of iris wounds was undertaken by Daniel[3] who performed iridectomies in rabbits and examined histologically the eyeballs at various periods following operation. From her work it is clear that the iris of rabbits as well does not show any tendency to form scar tissue.

To investigate this unusual lack of proliferation of cells of the iris following injury, tissue culture studies of adult human iris were undertaken in a previous study.[4] It was found that all the cellular elements of the iris proliferated in tissue culture except for those of the blood vessels. However, the latent period of the outgrowth of cells was very long and the rate of growth slow.

If iris tissue is able to grow in tissue culture what then is the reason for the lack of proliferation in vivo of cells of the iris following injury? It is possible that the aqueous humor inhibits cell growth in vivo following injury by mechanically removing through its flow the irritant necessary for cell proliferation. On the other hand, the aqueous humor may contain a substance which actively inhibits cell growth. Evidence for the latter assumption is found in the work of Stone.[5] He demonstrated that the potentiality of the iris of salamanders to generate lens tissue appears to be inhibited to a certain extent by aqueous.

In order to investigate further the suggestion that aqueous is able to inhibit the growth of cells the following tissue culture studies were undertaken.

MATERIALS AND METHODS

Fibroblasts derived from the hearts of eight-day-old chicken embryos were cultured in hanging drop cultures at 37.5°C. The medium consisted of one drop of fowl plasma and one drop of chicken embryonic extract. Cultures which grew vigorously were transferred twice in succession into fresh medium every second day. The fibroblasts of the second subpassage were divided into equal parts (sister cultures). One part was used for the experiment and the other for the control. These cultures were transferred into Maximow double cover slides as lying drops. The experimental medium consisted of one drop of fowl plasma, two drops of rabbit aqueous humor solution, and one

* From the Department of Ophthalmology, Hadassah-University Hospital, and the Department of Experimental Pathology (Cancer Research Laboratories), The Hebrew University-Hadassah Medical School.

drop of diluted chick embryo extract (third fraction—7.5-percent solution of the original concentrated embryonic extract) at a pH of 7.5. To the medium of the control two drops of Tyrode's solution were added instead of aqueous. The cultures were measured after three to five days with the help of Edinger's projectoscope and their size plotted graphically. Part of the cultures were fixed in Carnoy solution and stained with hematoxylin or Giemsa stain for histologic examination.

In a number of experiments mesentery and iris of adult rabbits were used. These tissues were grown either in Maximow slides as lying drops or in D3.5-mm. Carrel flasks. Cultures of the first or second subpassages were used for the experiments. In the experimental series the medium in the Maximow slides was the same as the one described above. The medium of the Carrel flasks contained 0.3 cc. fowl plasma, 0.6 cc. Earl's saline, and 0.3 cc. rabbit aqueous, and one drop of very diluted chick embryonic extract. To the control cultures 0.3 cc. of Tyrode's solution was added instead of the aqueous. The cultures in the Carrel flasks were kept at 37.5°C. for seven to 10 days without changing the medium. Part of the cultures were fixed in Carnoy solution for histologic examination.

Observations

Effect of aqueous humor on cultures of chicken fibroblasts

Forty-three pairs of cultures were included in this experiment. In every culture where aqueous had been added, the area of outgrowth was definitely smaller than in the control cultures. The average of the area of outgrowth of the experimental cultures was 69 ± 6 percent of the area of the control cultures, indicating a significant inhibition of growth (graph 1).

In some of the cultures containing aqueous not only was the area of outgrowth reduced but also the form of the cells was affected. The cells showed signs of degeneration, such as vacuolization of the cytoplasma and a tendency to round up (figs. 1 and 2). In some cases disintegration of cells was observed.

Effect of aqueous humor on cultures of rabbit mesentery and iris

Twenty-five pairs of cultures of mesentery and eight pairs of cultures of iris were used for this experiment. The area of outgrowth of the cultures containing aqueous was in most instances so small that no measurements could be made. The outwandering cells showed definite signs of degeneration such as vacuolization of the cytoplasm and rounding up of the cells followed rapidly by death of the cell (figs. 3, 4, 5, and 6).

Discussion

While aqueous humor has occasionally been used in tissue culture media, quantitative evaluation of its effect on the growth of cells has not been reported.

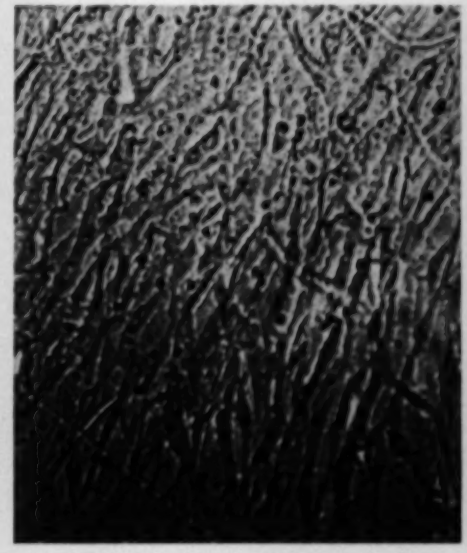
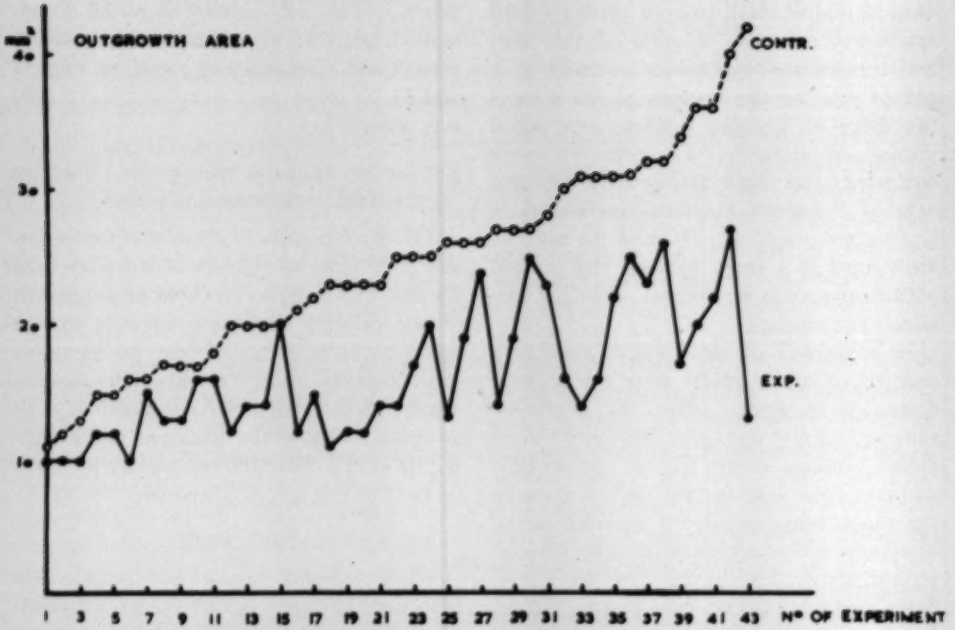


Fig. 1 (Kornblueth and Tenenbaum). Control culture. Third passage chicken fibroblasts in Maximow lying drop culture. (Three days old. ×140.)



Graph 1 (Kornblueth and Tenenbaum). Effect of aqueous humor on the area of outgrowth of chick fibroblasts in tissue culture. The experiments are arranged in order of increasing size of area of outgrowth of the controls.

Fig. 2 (Kornblueth and Tenenbaum). Sister culture of Figure 1 grown in a medium containing aqueous humor showing rounding up of the cells, vacuolization, and granulation of the cytoplasma (×140.)

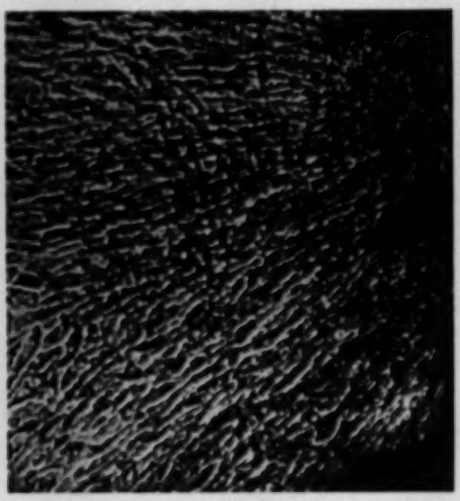


Fig. 3 (Kornblueth and Tenenbaum). Control culture. Second passage fibroblasts derived from rabbit mesenterium in Carrel flask. (Four days old. ×140.)

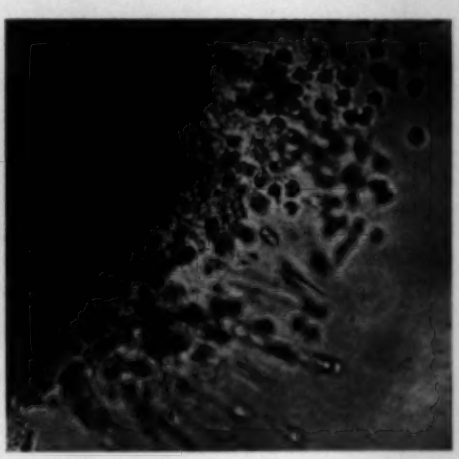


Fig. 4 (Kornblueth and Tenenbaum). Sister culture of Figure 3 grown in a medium containing aqueous humor. Note small area of outgrowth and degeneration of cells. (×140.)

Snell and Favata[6] claimed that various tissues could be grown in tissue culture equally well when the usual media were replaced in whole or in part with aqueous humor. However, Albrink and Wallace[7] reported that fragments of freshly explanted chick embryo hearts bathed in 100 percent aqueous humor did not show any growth. There was only migration of cells for three days followed by slow disintegration of the marginal cells. They also compared the growth of chick fibroblasts in media with and without aqueous. The growth of cells seemed superior in the presence of aqueous, but the two different media were not strictly comparable. Furthermore, the media contained embryonic extract whose power to stimulate growth might well have overshadowed the inhibitory effect of the aqueous. In our experiments the influence of the embryonic extract was reduced by using a highly diluted solution (7.5 percent of the original embryonic extract).

Goldhaber et al.[8] observed good growth of mouse sarcoma for four days only in a tissue culture medium containing aqueous humor and chicken plasma. Later on the cells became granular and disintegrated.

Fig. 5 (Kornblueth and Tenenbaum). Control culture. First passage rabbit iris in Carrel flask. (Nine days old. ×140.)

An inhibitory effect of aqueous may be the cause for the lack of wound healing in aseptic wounds of the iris. The reason that various tissues planted in the anterior chamber may continue to live if not to grow is that hardly any inflammatory reaction is induced by the transplantation.[9] The only tis-

Fig. 6 (Kornblueth and Tenenbaum). Sister culture of Figure 5 grown in a medium containing aqueous humor. Only single cells migrated from the explant. (×140.)

sues which actively grow in the anterior chamber are malignant tumors and fetal tissues[10] which show autonomous growth. It is possible that such tissues may be able to neutralize the inhibitory substance in the aqueous humor.

The proliferation of blood vessels also seems to be inhibited by aqueous. Thus, usually no blood vessels grow into a filtering trephine bleb and no blood vessels are found in the immediate surroundings of a corneal fistula.

In addition, epithelial invasion of the anterior chamber is rare and was found only in one of 1,625 perforating wounds[11] although many epithelial cells capable of proliferation within the eye may be implanted by the trauma. It was shown clinically[12] and experimentally[13] that epithelial invasion of the anterior chamber occurs only in cases where healing of the limbal wounds is delayed, giving rise to the formation of plasmoid aqueous.

Thus the experiments presented here which show inhibition of the growth of chick and rabbit fibroblasts and of rabbit iris by aqueous, are supported by clinical observations and experimental work.

Summary and Conclusions

Experimental evidence is presented which shows that aqueous humor inhibits the growth of chick and rabbit fibroblasts and rabbit iris in tissue culture. This growth inhibitory effect of the aqueous humor may be the cause for the lack of wound healing in aseptic wounds of the iris in man and animals.

Department of Ophthalmology,
Hadassah-University Hospital.

Acknowledgment

The authors are indebted to Mrs. R. Nevad for technical assistance, to Dr. G. Goldhaber for performing the calculations, and to Mr. J. Kuffler for drawing the graph.

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FIELD FINDINGS IN FUNCTIONAL DISEASE*

Report of 63 cases

William O. Linhart, M.D.
Pittsburgh, Pennsylvania

Some correlation between functional disease and abnormal field variation has been generally conceded. Field changes characteristic of hysteria, psychoneurosis, and chronic fatigue states are frequently seen in practice and are described in the various textbooks. In practice it is difficult to evaluate the patient because, frequently, little is known about his mental or physical status. Even though the ocular findings suggest functional disease, there remains uncertainty of diagnosis.

The influence of the psychic factor on the visual apparatus is likely to become apparent during periods of stress and strain—in the youngster, pressure from work in school or conflict at home; in the middle aged, pressure of business, social, marital, or financial matters; and, in the aged, the problems of adaptation to life—all are important factors influencing vision. These stress factors vary from day to day and month to month, as do the mental changes and field findings. The psychic factors can be reduced by changes in environment or by the use of hypnosis or such drugs as the barbiturates. It has been suggested by Benet and Janet, as cited by deSchweinitz,[1] that patients suffering from hysterical amaurosis, when placed under hypnotic influence, can recall what they saw before the hypnotic state was induced.

Peter[2] described three types of changes characteristic of hysterical amblyopia:

1. Concentric contracture of fields with or without central amblyopia.
2. Development of tubular fields.
3. Reversal of color fields.

He also stated that any variation in the field observed in organic disease of the visual tract may be encountered in hysterical disease.

Frequently, the most experienced ophthalmologist has great difficulty in segregating the malingerer from the patient with organic ocular disease, or even more difficulty from the patient with functional ocular disease whose visual deficiency is not on a voluntary conscious basis. The malingerer can usually be differentiated by various office tests, using prisms and colored filters. These tests have no value in appraising the true visual deficiency in mental disease, which lies in the unconscious. Spaeth[3] has discussed this subject at length and excellently.

In 1943, Mahoney and I[4] made a complete physical and mental study of 13 cases of hysterical amblyopia in soldiers during their first three months of Army life. Most of these men were found to have an IQ rating (Benet-Simon Test) below 90, indicating inferior intelligence and putting them into Kretschmer's apt classification of "having a stunted psyche."

Although discussions of field in hysterical amblyopia seem to have more general interest, the irregular and unevenly contracted peripheral field findings of psychoneurotic neurasthenia are probably more commonly seen in practice. As the test is prolonged, these patients show the fatigue or spiralling decrease.

In neurasthenic field procedures, it is quite important that all fields be taken with, as much as possible, the same preliminary instructions and same amount of time, and that the first reading be recorded—later findings can then be compared.

Present study

The patients in this series were all selected from the Pittsburgh Diagnostic Clinic on the basis of their field findings; the records of

* From the Department of Ophthalmology, University of Pittsburgh. Read before the Section of Ophthalmology, Pennsylvania State Medical Society, September, 1955.

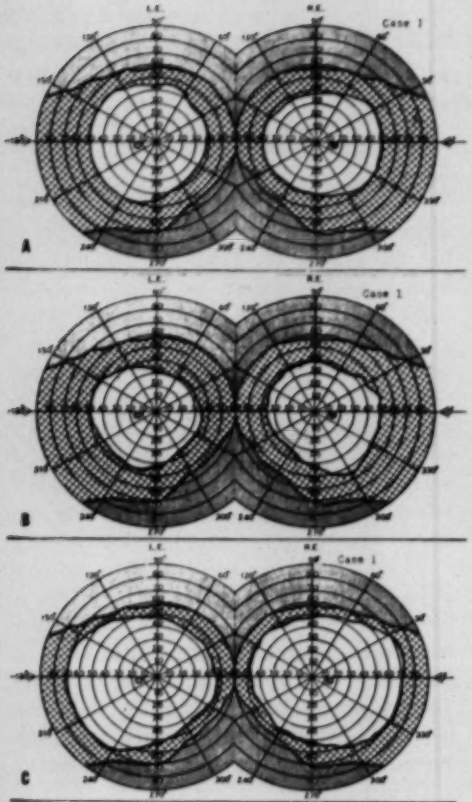


Fig. 1 (Linhart). *Case 1,* a girl, aged 16 years. (A) Psychoneurosis with anxiety. (B) Three months later. (C) Six months later; mental condition improved.

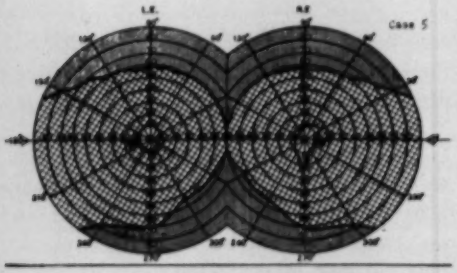


Fig. 5 (Linhart). *Case 5,* a woman, aged 58 years. Nervous tension state.

Fig. 6 (Linhart). *Case 6,* a woman, aged 70 years. Senile depression.

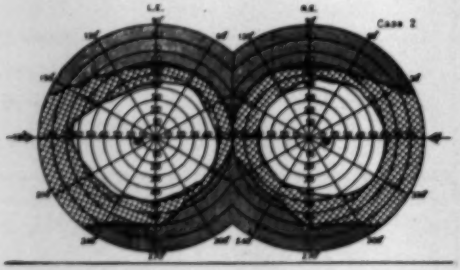


Fig. 2 (Linhart). *Case 2,* a woman, aged 37 years. Schizophrenia.

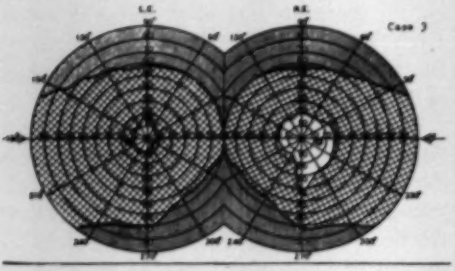


Fig. 3 (Linhart). *Case 3,* a woman, aged 66 years. Psychoneurosis.

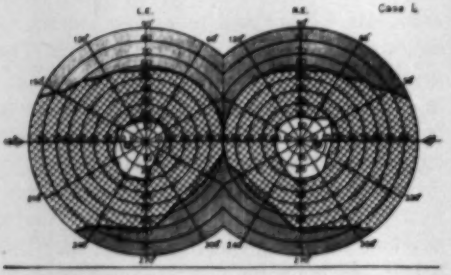
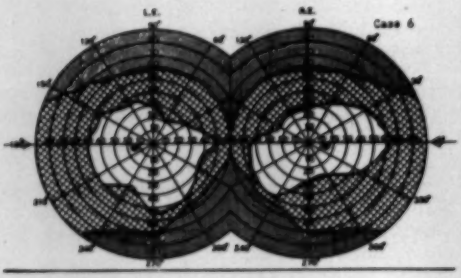


Fig. 4 (Linhart). *Case 4,* a man, aged 45 years. A fatigue state.



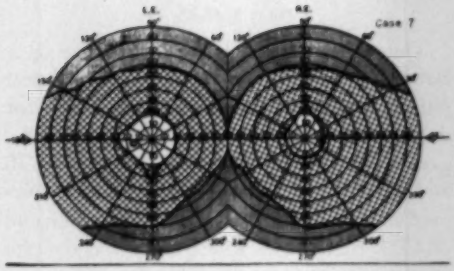


Fig. 7 (Linhart). *Case 7,* a woman, aged 27 years. Psychoneurosis with anxiety.

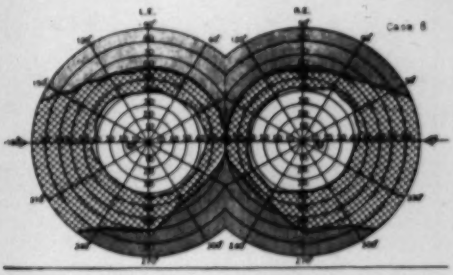


Fig. 8 (Linhart). *Case 8,* a man, aged 59 years. Anxiety state.

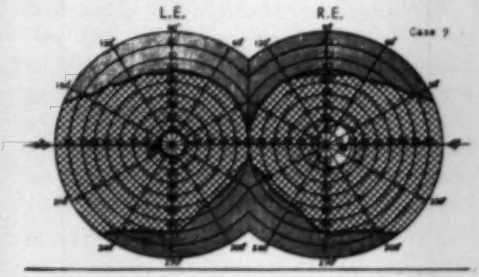


Fig. 9 (Linhart). *Case 9,* a woman, aged 24 years. Ocular hysteria.

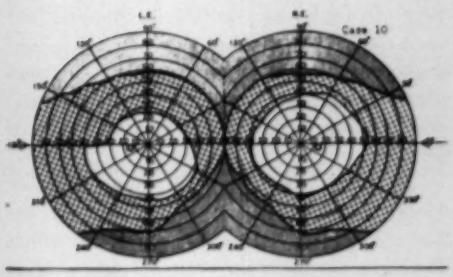


Fig. 10 (Linhart). *Case 10,* a woman, aged 62 years. Nervous tension state.

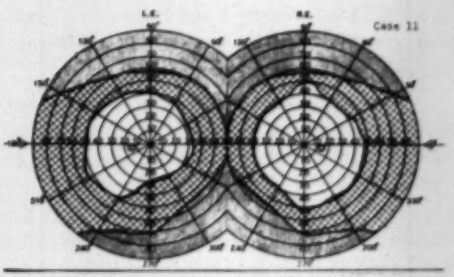


Fig. 11 (Linhart). *Case 11,* a woman, aged 51 years. Histamine headache.

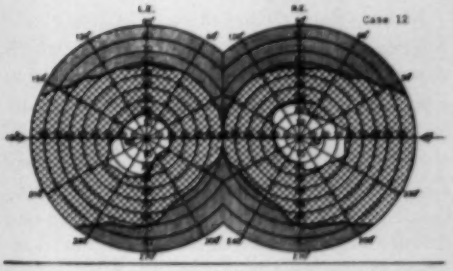


Fig. 12 (Linhart). *Case 12,* a man, aged 50 years. Psychoneurosis.

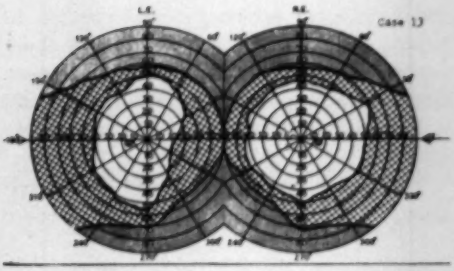


Fig. 13 (Linhart). *Case 13,* a man, aged 51 years. Psychoneurosis.

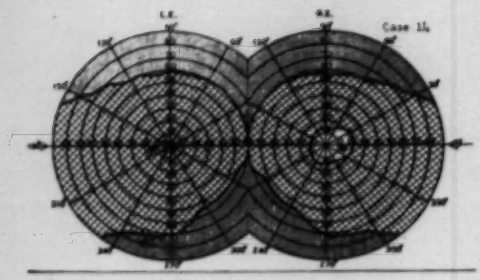


Fig. 14 (Linhart). *Case 14,* a man, aged 47 years. Ocular hysteria.

their physical and psychiatric examinations were then studied. This procedure provided a group made up of persons of all ages whose ocular symptoms were not the basic investigating point. Table 1 is a summary of the cases.

Of the 63 patients, 36 were females, which is a normal percentage rate for the average clinic or ophthalmologist's office. The ages varied from 16 to 70 years. Most patients were in the 40 to 55-year age group and, interestingly, most of the men were in this group.

In 57 consultations, the psychiatrist made definite mental functional diagnoses, which varied from fatigue states and migraine to schizophrenia. Most patients exhibited some form of nervous tension with superimposed anxiety. Psychoneurosis was commonly found. Of the six cases in which no functional mental diagnosis was made, three had definite organic brain disease. Cerebral vascular disease was found in Cases 20 and 30 but no cerebral vascular accident was evident. In Case 32 cerebral-spinal syphilis was proven. In Case 37 no organic or functional mental diagnosis could be made. Case 61, in which early brain tumor was suspected, when examined after six months showed no evidence of tumor.

The physical findings revealed nothing of particular note. They were those of the average patient referred to the clinic for evaluation.

Field findings

The field examinations were taken on a Brombach perimeter; 0.5-degree form test objects were used routinely if the vision for distance was better than 20/50 and 1.5-degree objects if the vision was between 20/50 and 20/200. A 3.0 degree test object was used if the vision was between 8/200 and 20/200. In all cases where there was definite contracture and spiralling, a 3.0-degree test object was used in addition to those of other size.

Excluding the tubular fields, about half the fields showed some spiralling. This spiralling tendency was worse in states of high nervous tension and fatigue. In almost all cases the size of the test object made very little difference in the size of the field. In addition, if the field was large enough to include the blindspot, the normal blindspot was enlarged. In Case 1 it is interesting to note the changes which took place in the field over several months.

Tubular fields were found in eight cases. All of these fields were less than 15 degrees in size. Two different-sized form test objects and a red test object were used; all the resulting fields were the same size.

The correctible vision was 20/20 in all but nine cases. In one of these cases a chorioretinal scar in one eye reduced the vision to peripheral only. In the remaining eight cases, no organic lesion was found and it was assumed, considering the other findings, that both central and peripheral vision were reduced.

In 34 cases no particular ocular pathologic change was present. If some pathologic eye condition were present, it was chronic in nature. The refraction errors were those found in the average clinic patient. The one large refractive error was astigmatic and was found in a patient with an anxiety state.

The ocular symptoms showed great variation, the most common symptoms were

TABLE 1

CASE SUMMARIES

Case No.	Sex	Age (yr.)	Mental Diagnosis	Fields*	Physical	Vision without Correction	Vision with Correction	Ocular Pathology	Refractive Error	Ocular Symptoms	Occupation
1	F	16	Psychoneurosis with anxiety	M C C	Dental caries	OD 20/200 OS 20/150	OD 20/70 OS 20/50	None	Mild astigmatism	Blurring on ocular effort	Student
2	F	37	Schizophrenia & borderline mental defective	S C C	1—large uterine fibroid 2—internal hemorroids	OD 20/40 OS 20/50	OD 20/20 OS 20/20	Exophthalmos	Slight myopia	Nervous, hurting of eyes	Housewife
3	F	66	Psychoneurosis with hypochondriasis	M C C some spiralling	1—widespread degenerative arthritis, moderate with superimposed psychogenic rheumatism 2—otitis externa, mild 3—plantar callosity	OD 20/150 OS 20/200	OD 20/20 OS 20/20	Occasional punctate corneal erosions	Moderate hyperopia	Eyes burn	Housewife
4	M	45	Fatigue state	Tubular	1—hypothyroidism 2—xanthelasma (with hypercholesterolemia, probably secondary to above)	OD 20/70 OS 20/70	OD 20/20 OS 20/20	None	Moderate hyperopia	Eyes tire easily	Department Head
5	F	58	Nervous tension state with superimposed anxiety	Tubular	1—stenosis of urethral meatus 2—degenerative arthritis of cervical spine, with associated fibromyositis 3—exogenous obesity	OD 20/100 OS 20/70	OD 20/20 OS 20/20	Moderate sclerosis of retinal arterioles	Moderate astigmatism	Tremor left eye. Bifocal difficulty	Housewife
6	F	70	Senile depression	M C C marked spiralling	1—generalized arteriosclerosis w/arteriosclerotic heart disease, well compensated 2—generalized osteoporosis, senile type 3—painless hematuria, cause undetermined	OD 20/150 OS 20/150	OD 20/20 OS 20/20	None	None	Dryness right eye for 1 yr.	None
7	F	27	Psychoneurosis anxiety	M C C some spiralling	1—neuromuscular pain, type unknown	OD 20/20 OS 20/20	OD 20/20 OS 20/20	None	None	Dizzy spells	Housewife
8	M	59	Anxiety state	M C C marked spiralling	1—postconcussion syndrome 2—nerve deafness, bilateral moderately severe 3—chronic cholecystitis	OD 20/100 OS 20/200	OD 20/20 OS 20/20	1—moderate arteriosclerotic retinopathy 2—early senile cataracts	Moderate hyperopia	Occasional left-sided headaches	Laborer
9	F	24	Ocular hysteria	Tubular	1—exogenus obesity, severe with secondary amenorrhea 2—ulcers of nasal septum	OD 20/40 OS 20/40	OD 20/20 OS 20/20	None	Mild myopia	Eyes burn & cause headaches	Laborer
10	F	62	Nervous tension state	M C C	1—psoriasis involving periorbital region right elbow & perineal region secondarily infected	OD 20/100 OS 20/50	OD 20/20 OS 20/20	Allergic dermatitis of lids	Compound hyperopic astigmatism	Tiring & burning	Housewife
11	F	51	Histamine type headache	M C C	1—lower urinary tract abnormalities	OD 20/100 OS 20/100	OD 20/20 OS 20/20	Moderate sclerosis retinal arterioles	Moderate hyperopia	Headaches on arising with poor vision	Social Worker
12	M	50	Psychoneurosis mixed type	M C C	1—probable hydrops of left labyrinth 2—chronic hepatitis alcoholic	OD 20/70 OS 20/50	OD 20/20 OS 20/20	None	Moderate hyperopia	Headaches ten years. Never could wear glasses	Miner

* FIELDS: MCC means "moderate concentric contracture"; SCC means "slight concentric contracture."

TABLE 1—(*continued*)

Case No.	Sex	Age (yr.)	Mental Diagnosis	Fields*	Physical	Vision without Correction	Vision with Correction	Ocular Pathology	Refractive Error	Ocular Symptoms	Occupation
13	M	51	Psychoneurosis	M C C marked spiralling	1—hypothyroidism [illegible] 2—perceptive deafness with depressed labyrinthine sensitivity	OD 20/40 OS 20/40	OD 20/20 OS 20/20	None	Mild hyperopia	Poor vision with glasses	Skilled laborer
14	M	47	1—Possible intracranial expanding lesion 2—Ocular hysteria	Tubular	1—rheumatic heart disease, minimal mitral insufficiency, well compensated 2—Essential hypertension, benign	OD 20/50 OS 20/100	OD 20/20 OS 20/20	None	Moderate myopia	Aching left eye for 2 mo.	Store Operator
15	F	60	Illiterate & borderline mental defective	S C C	1—diabetes mellitus, moderate-severe 2—varicose veins 3—vasomotor instability, endocrine type with postinfectious aggravation	OD 20/70 OS 6/200	OD 20/20 OS 20/60	Corneal scar left eye, amblyopia exanopsia, left eye	Hyperopic type, moderately large	Intermittent visual blurring	Housewife
16	M	51	Reactive depression	M C C	1—essential hypertension, benign phase, mild 2—dental caries	OD 20/30 OS 20/25	OD 20/20 OS 20/20	Very early cataracts	Slight astigmatism	Dizziness on reading	Salesman
17	M	29	Anxiety neurosis (cardiac neurosis)	S C C	1—irritable duodenum functional 2—pruritus ani with cryptitis	OD 20/20 OS 20/20	OD 20/20 OS 20/20	Mild marginal blepharitis	None	Bitemporal headaches at any time	Engineer
18	F	60	Migraine	M C C	1—nonthrombopenic purpura 2—essential hypertension	OD 20/30 OS 9/200	OD 20/20 OS 20/25	Exophthalmos, left eye	Myopia mild right eye. Hyperopia large, left eye	Protruding left eye & headaches	Housewife
19	M	42	No functional mental diagnosis	M C C	1—possible diencephalic disease	OD 20/45 OS 20/50	OD 20/20 OS 20/20	Mild conjunctivitis	Mild myopia	Attacks of headaches, not particularly ocular	Merchant
20	M	50	No functional diagnosis	Marked irregular contracture	1—cerebral lesion, possibly vascular	OU 20/200	OU 20/20	Slight exophoria	Moderate hyperopia	Headaches on ocular effort	Machinist
21	F	47	None definite except ocular neurosthenia	Marked irregular contracture	1—essential hypertension 2—chronic cervicitis retroversion of the uterus and trichomonas vaginalis infection 3—degenerative arthritis	OD 20/50 OS 20/45	OD 20/20 OS 20/20	Moderate hypertensive ocular fundi	Mild hyperopia	Poor visual endurance	Housewife
22	F	39	Anxiety state post-traumatic	M C C marked spiralling	1—periarticular and intramuscular fibrositis, entire back, post-traumatic 2—perceptive deafness, mild, bilateral 3—relaxation of pelvic floor	OD 20/40 OS 20/25	OD 20/30 OS 20/20	Central chorioretinal scar	Slight hyperopia	Poor focusing right eye	Housewife
23	F	35	Chronic nervous tension and anxiety state	M C C	1—chronic dyspepsia and pyloro-spasm 2—possible cholelithiasis	OD 20/25 OS 20/50	OD 20/25 OS 20/25	None	Slight hyperopia	None	Housewife
24	F	21	None definite except ocular neurosthenia	M C C	1—osteoarthritis of lumbar and dorsal areas 2—pulmonary tuberculosis minimal stabilized	OD 20/100 OS 20/200	OD 20/25 OS 20/25	Occasional vitreous opacity	Moderate hyperopia	Spots in eyes, recurrent in eyes	Housewife
25	F	73	None except ocular neurosthenia	M C C	1—varicose ulcer, left leg 2—large prolapsing hemorrhoids 3—diverticulosis of the colon	OD 20/200 OS 20/150	OD 20/20 OS 20/20	Mild punctate corneal erosions & chronic mild blepharitis	Moderate hyperopia	Eyes burning constantly	Housewife

TABLE 1—(*continued*)

Case No.	Sex	Age (yr.)	Mental Diagnosis	Fields*	Physical	Vision without Correction	Vision with Correction	Ocular Pathology	Refractive Error	Ocular Symptoms	Occupation
26	M	43	Psychoneurosis	Tubular	1—possible intracranial expanding lesion 2—dental sepsis	OD 20/200 OS 20/150	OD 20/25 OS 20/25	None	Moderate hyperopia	Eyes ache constantly	Laborer
27	F	58	Chronic fatigue	M C C	1—gastroenterostomy with recurrent obstruction 2—diabetes mellitus, uncontrolled 3—chronic pyelonephritis, right side 4—arteriosclerotic heart disease with bundle branch block	OD 12/200 OS 20/45	OD 20/100 OS 20/35	Moderate arteriosclerotic	Moderate hyperopia	Spots before eyes	Housewife
28	M	45	Anxiety state	S C C	1—chronic low-grade nasopharyngitis & sinusitis 2—serous otitis media secondary to above	OD 20/25 OS 20/25	OD 20/20 OS 20/20	Very early senile cataracts	Mild astigmatism	Vision blurring for for 1 mo.	Supervisor
29	F	29	Psychoneurosis	Tubular	1—mild hypothyroidism 2—retroversion of the uterus	OD 20/20 OS 20/20	OD 20/20 OS 20/20	Mild exophoria	Mild myopia	Ocular fatigue Difficulty focusing	Housewife
30	F	60	None	M C C	1—cerebral vascular disease, degenerative 2—essential hypertension	OD 16/200 OS 2/200	OD 20/20 OS 20/20	Mild arteriosclerotic retinopathy with amblyopia exanopsia, left eye	Moderate hyperopia	None	Housewife
31	F	37	Hysteria	S C C	1—functional aphonia	OD 20/20 OS 20/20	OD 20/20 OS 20/20	Mild hypertensive fundi	Mild hyperopia	None	Housewife
32	M	59	Tertiary lues, with central nervous system involvement	M C C	1—labyrinthine vertigo probably secondary to hydrops of left labyrinth 2—stricture, unrethral meatus 3—seborrhoic dermatitis of scalp	OD 20/25 OS 20/30	OD 20/20 OS 20/20	Tertiary syphilis	Moderate hyperopia	Poor vision	Clerk
33	M	58	Psychoneurosis, chronic anxiety state	M C C	1—degenerative process, pyramidal tract, bilateral mild, type undetermined	OD 20/40 OS 20/40	OD 20/20 OS 20/20	1—slight exophthalmos 2—early senile cataracts	Mild myopia	None	Merchant
34	F	40	Anxiety attacks	M C C some spiralling	1—possible gall bladder disease	OD 20/20 OS 20/25	OD 20/20 OS 20/20	Trichinosis right upper lid	Moderate hyperopia	Blurring right eye since child Pain right eye for 1 wk.	Housewife
35	M	32	Probable ocular hysteria	M C C	1—labyrinthine vertigo 2—suppurative tonsillitis	OD 20/20 OS 20/20	OD 20/20 OS 20/20	1—ptosis left upper 2—right hyperphoria	None	None ocular. Dizziness 3 yr.	Maintenance Man
36	M	75	Ocular neurasthenia	M C C	1—mixed type deafness bilateral, severe with associated vascular vertigo 2—third degree benign prostatic hypertrophy	OD 20/200 OS 20/100	OD 20/25 OS 20/25	Early cataract left eye	Moderate hyperopia	None ocular. Dizziness	Meat packer
37	M	56	None	M C C	1—angina pectoris (coronary insufficiency) 2—perforation of left ear drum w/chronic otitis media	OD 20/25 OS 20/40	OD 20/20 OS 20/20	Very early senile cataracts	Slight hyperopia	Frontal headaches after reading	Miner

TABLE 1—(*continued*)

Case No.	Sex	Age (yr.)	Mental Diagnosis	Fields*	Physical	Vision without Correction	Vision with Correction	Ocular Pathology	Refractive Error	Ocular Symptoms	Occupation
38	M	69	Central nervous system degeneration on arteriosclerotic basis	M C C marked spiralling	1—degenerative fibromyositis of hips & both legs 2—benign prostatic hypertrophy 3—arteriosclerotic & hypertensive heart disease	OD 20/70 OS 20/70		Severe sclerosis retinal arterioles	Moderate hyperopia	Vision diminishing	Retired
39	F	37	Atypical migraine	M C C	1—suppurative maxillary sinusitis, left	OD 20/25 OS 20/30	OD 20/20 OS 20/20	Benign melanoma of choroid	Mild astigmatic	Continuous frontal headaches for 6 mos.	Housewife
40	F	43	Anxiety state	M C C some spiralling	1—coccydynia 2—facial dysesthesia probably vascular	OD 8/200 OS 8/200	OD 20/20 OS 20/20	Left hyperphoria	Large astigmatic	Weakness right side of face, no ocular symptoms	Housewife
41	M	35	Psychoneurosis mixed type	M C C	1—external otitis, chronic quiescent 2—catarrhal rhinitis	OD 20/40 OS 20/50	OD 20/20 OS 20/20	Chronic follicular conjunctivitis	Mild astigmatic	Pulling of eyes	Clerk
42	M	57	Questionable ocular hysteria	M C C	1—narrowing of sigmoid due to diverticulitis 2—internal hemorrhoids 3—organic heart disease with angina pectoris	OD 20/100 OS 20/200	OD 20/20 OS 20/20	Multiple foreign bodies left eye	Moderate myopic	Scratching of left eye 3 mo. Ocular injury 3 yr. ago	Miner
43	F	44	Ocular hysteria	Tubular	1—degenerative arthritis lumbar spine with referred pain 2—mild trigonitis and posterior urethritis	OD 20/70 OS 20/40	OD 20/20 OS 20/20	None	Mild hyperopia	Vision weak for 1½ yr.	Housewife
44	M	61	Atypical migraine (aggravated and distorted by nervous tension)	M C C	1—left maxillary sinusitis	OD 20/30 OS 20/30	OD 20/20 OS 20/20	Moderate sclerosis retinal arterioles	Mild astigmatic	Left sided headaches for 10 yr.	Laborer
45	M	46	Chronic vascular headache probably	M C C	1—perceptive deafness bilateral, severe	OD 20/20 OS 20/25	OD 20/20 OS 20/20	None	Mild myopic	Occipital headaches No ocular symptoms	Welder
46	F	61	Nervous tension state with superimposed anxiety	S C C	1—undernutrition & avitaminosis, dietary 2—extensive diverticulosis associated with quiescent, chronic, ulcerative collitis	OD 20/70 OS 20/200	OD 20/20 OS 20/20	Moderate severe sclerosis retinal arterioles	Moderate hyperopic	Three attacks iritis, right eye	Housewife
47	F	63	Functional indigestion	Tubular	1—underweight	OD 18/200 OS 18/200	OD 20/20 OS 20/20	None	Moderate hyperopic	Poor vision. Dizziness	Housewife
48	M	26	Anxiety state	S C C some spiralling	1—none	OD 20/20 OS 20/20	OD 20/20 OS 20/20	None	Mild astigmatic	Burning of eyes	Contractor
49	F	16	Convulsive state (nature)	M C C	1—allergic asthma and allergic sinusitis	OD 20/200 OS 20/70	OD 20/20 OS 20/20	None	Myopia	Frontal headaches	Student
50	F	45	Migraine with labyrinthine equivalent	M C C	1—laceration of pelvic floor with associated cystocele, rectocele, & second degree prolapse of the uterus 2—probable dental pulp infection	OD 20/30 OS 20/25	OD 20/20 OS 20/20	None	Myopic astigmatism	Recurrent left side headaches	Seamstress

TABLE 1—(*continued*)

Case No	Sex	Age (yr.)	Mental Diagnosis	Fields*	Physical	Vision without Correction	Vision with Correction	Ocular Pathology	Refractive Error	Ocular Symptoms	Occupation
51	F	38	Nervous tension state	S C C	1—essential hypertension neurogenic phase 2—possible incipient thyrotoxicosis 3—exogenous obesity	OD 20/20 OS 20/20	OD 20/20 OS 20/20	Slight hyperphoria	None	None	Housewife
52	F	37	Migraine	M C C	1—mild essential hypertension 2—internal hemorrhoids, moderately severe with anal fissuring	OD 20/50 OS 20/60	OD 20/20 OS 20/20	None	Myopic	Left side headaches with vomiting	Housewife
53	F	52	Nervous tension state with chief ocular symptoms	M C C	1—arteriosclerotic and hypertensive heart disease 2—probable cholelithiasis	OD 20/70 OS 20/100	OD 20/20 OS 20/20	Mild chronic conjunctivitis	Hyperopic	Red eyes & irritated for 10 yr.	Housewife[a]
54	F	60	Psychoneurosis mixed type	S C C marked spiralling	1—essential hypertension moderately severe 2—laceration of the pelvic floor	OD 20/50 OS 1/200	OD 20/20 OS 5/200	Occlusion central retinal vein	Hyperopic	Poor vision left eye	Housewife
55	M	63	Labyrinthine vertigo, probably arteriosclerotic in origin	M C C	1—external and internal hemorrhoids moderately severe 2—bilateral apical pulmonary fibrosis, probably representing healed tuberculosis	OD 20/50 OS 20/45	OD 20/20 OS 20/20	None	Hyperopic	Dizzy spells	Laborer
56	M	53	Psychoneurosis mixed type	M C C some spiralling	1—pulmonary tuberculosis right apex, probably inactive	OD 20/40 OS 20/35	OD 20/20 OS 20/20	Melanoma skin of lids	Hyperopic	Frontal headaches	Miner
57	M	51	Psychoneurosis obsessive compulsive type	M C C	1—toxic tonsillitis 2—conductive deafness left ear 3—internal hemorrhoids, large prolapsed 4—benign prostatic hypertrophy with chronic prostatitis	OD 20/100 OS 20/20	OD 20/50 OS 20/20	Chronic keratitis	Hyperopic astigmatism	Poor vision right eye	Salesman
58	F	54	Nervous tension state	S C C	1—essential hypertension 2—obesity 3—first degree hydronephrosis, right side 4—laceration of pelvic floor (w/rectocele & beginning prolapse of uterus)	OD 20/100 OS 20/70	OD 20/20 OS 20/20	Mild hypertensive fundi	Hyperopic	Frontal headaches	Housewife
59	F	55	Nervous tension state, with anxiety	S C C	1—allergic rhinitis, mild 2—varicose veins, both legs	OD 20/200 OS 20/200	OD 20/25 OS 20/40	Mild exophthalmos probably familial	Small hyperopic astigmatism	Recurrent lid swelling	Housewife
60	F	34	Vasomotor rhinitis from tension state	S C C	1—erosion of the cervix	OD 20/40 OS 20/70	OD 20/20 OS 20/20	None	Mixed astigmatism	Frontal headaches	Housewife
61	M	38	Brain tumor suspect	M C C marked spiralling	1—negative	OD 20/20 OS 20/20		None	None	Twitching of lid	Machinist
62	M	54	Probable cerebral vascular spasm	M C C	1—arteriosclerotic heart disease & peripheral vascular insufficiency 2—mild essential hypertension	OD 1/200 OS 20/25	OD 1/200 OS 20/20	Old chorioretinal scar	Hyperopic astigmatism	Poor vision right eye	Mechanic
63	F	41	Anxiety and nervous tension state	S C C some	1—functional spasm of bowel or left upper urinary tract 2—relaxation of perineum	OD 20/25 OS 20/50	OD 20/20 OS 20/20	Horner's syndrome	Myopic	Poor vision	Housewife

burning of eyes and blurring of vision on ocular effort. Six patients showed no ocular symptoms.

The most common occupation was that of housewife, under which 29 patients were classified. There were executives, professional people, salesmen, and so forth. One patient was a student and two had no occupation. It may be seen that most of these patients were busily occupied people.

Summary

Sixty-three cases of contracted fields, functional in type, were studied from all standpoints at the Pittsburgh Diagnostic Clinic. All of the cases were psychiatrically examined. In most of the cases psychiatric examination would have been done without the field findings suggesting it, while in the others psychiatric examination was requested after ocular examination.

The field findings which prompted functional diagnosis were:

1. Bilateral contracture of form fields with equal size on different test objects.
2. Bilateral spiralling contracture.
3. Bilateral contracture of fields with reversal of color fields or color fields equal to form fields.

The severity of the mental disease did not seem to be directly related to the amount of field involvement. Almost always, however, a number of ocular symptoms were present in the cases in which there was an appreciable amount of field contracture. The symptoms never included poor side vision but were usually related to those found in external eye diseases. The most common ocular symptoms were burning or foreign-body sensation. Complaints of related conjunctivitis were common.

Correctible vision of 20/20 in no way eliminates involvement of the field. Some of the worst cases of ocular hysteria with tubular fields had normal corrected vision.

Conclusions

1. Field examination is an important part of the physical, psychiatric, and ocular evaluation of the functional patient.
2. Field findings show a definite pattern in functional cases just as they do in organic cases.
3. Most mental cases with ocular symptoms show functional field changes, and routine fields on the so-called "neurotic patient" are important.
4. Most functional field changes are found in patients of middle age and are definitely related to mental stress.
5. Functional fields vary according to mental attitudes in the same individual but total recoveries are not common.
6. In addition to their underlying mental disease, patients with functional field contracture are not good employment risks; nor are they safe pedestrians or car drivers.

Medical Arts Building (13).

I am indebted to the staff of the Pittsburgh Diagnostic Clinic for full co-operation and particularly to the director, Dr. R. R. Snowden.

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IRRADIATION OF THE POSTERIOR OCULAR SEGMENT WITH RADIOACTIVE YTTRIUM*

FRANK W. NEWELL, M.D., AND PAUL V. HARPER, JR., M.D.
Chicago, Illinois
AND
AUNE KÖISTENEN, M.D.†
Helsinki, Finland

The delicate functional structure of the eye has created wide interest in superficial radiation with beta rays, which do not penetrate deeply. Focal area irradiation of the anterior segment of the globe by means of beta rays has been ably reviewed in recent years by Hughes,[1] Wilson,[2] and Iliff,[3] and Friedell and his associates.[4] Stallard[5] in a series of reports, has described the effects of radon seeds, radium discs, and cobalt 60 upon the posterior ocular segment in eyes containing retinoblastomas. There have been no reports concerning the effects of a pure beta-ray emitter upon the posterior ocular segment. Such a study is of clinical application because of the possibility of using point sources of irradiation in the treatment of small retinoblastomas and the retinal tumors of angiomatosis.

Prior to the invention of the cyclotron in 1931, and more recently nuclear chain reactors and piles, beta-ray emitters were limited to naturally occurring sources. At present a wide variety of elements with different physical and radioactive properties is available.

Yttrium^{90}, which was used in the study, is most familiar to ophthalmologists as the therapeutically effective portion of radioactive strontium. Strontium^{90} decays to yttrim^{90} by the emission of a beta particle having a penetration of but 0.35 mm. in tissue. Yttrium^{90} decays to zirconium^{90}, a stable isotope, by emitting a beta particle with a maximum energy of 2.3 mev (million electron volts) and a mean energy of 0.90 mev maximum. Penetration in tissue is less than nine mm. Yttrium^{90} has a half-life of 62 hours, so that it reaches 90-percent saturation activity after one week of irradiation in the pile. With a neutron flux of 3×10^{12} neutrons per cm.^{2} per second, this activity is about 0.5 mc. per mg. of Y_2O_3.

TECHNIQUE

Yttrium pellets, prepared and calibrated as described by Rasmussen, et. al.,[6] were superficially attached to the sclera in a series of male mongrel, pigmented rabbits. The animals were anesthetized with intravenous pentobarbital and topical tetracaine hydrochloride (Pontocaine). A medial and lateral canthotomy was done and the lids were retracted with sutures. The superior rectus muscle was then grasped, the eye was rotated downward, and an incision was made through the conjunctiva exposing the sclera. In a few animals a hinged scleral flap was made to contain the pellets but, in the majority, the pellets were placed underneath Tenon's capsule and the conjunctiva closed with no particular effort to hold the yttrium pellet in contact with the sclera. The radioactive pellet was placed in position by means of a spinal puncture needle, which was shielded with lead, and contained a stylet with which the pellet was expelled.

Ophthalmoscopic examination was carried out at weekly intervals postoperatively. The animals were killed with intravenous pentobarbital and the eyes removed at various time intervals following the implantation.

The eyes were fixed in formalin solution.

* From the Argonne Cancer Research Hospital and the Department of Surgery, the University of Chicago. This study was supported in part by Graduate Training Grant #2-B-5079 of the National Institute of Neurological Diseases and Blindness of the National Institute of Health, Public Health Service.

† International exchange student in ophthalmology.

Sections, 17 microns thick, were made, and every 10th section was stained with hematoxylin and eosin.

Results

Forty-one eyes were studied histologically. Of these there were no abnormal findings in 11. It was probable that in these eyes the yttrium pellet was dislodged from its insertion in the sclera and the posterior ocular segment received either too little radiation to cause histologic changes, or that the changes were too minute to be recognized. Our study concerns the remaining eyes in which histologic changes due to radiation were observed.

Acute radiation injury was observed in a series of eyes enucleated within 14 days after the insertion of the yttrium pellet. Graduated doses were not administered so that the minimal effective radiation was not observed except by measurement of the area of involvement in the affected eyes. Fixation of the eye causes unequal shrinkage of the choroid and the retina so that such measurements are extremely inaccurate.

The eyes of animals to which a 0.8-mc. pellet had been applied for 24 hours showed an acute radiation injury. The muscle and the sclera immediately adjacent to the pellet were markedly necrotized. The entire area was infiltrated with large numbers of polymorphonuclear cells which were also necrotic. The reaction was so severe that the sclera perforated in some animals. The choriocapillaris layer which in most normal animals is relatively inconspicuous became markedly dilated and there was rupture of the blood vessels.

No recognizable structure was evident in the retina in the area of most intense reaction. The layer of rods and cones was entirely destroyed and a homogenous pink-staining fluid substituted. Adjacent to the area of acute necrosis the external nuclear layer showed pyknosis and karyorrhexis

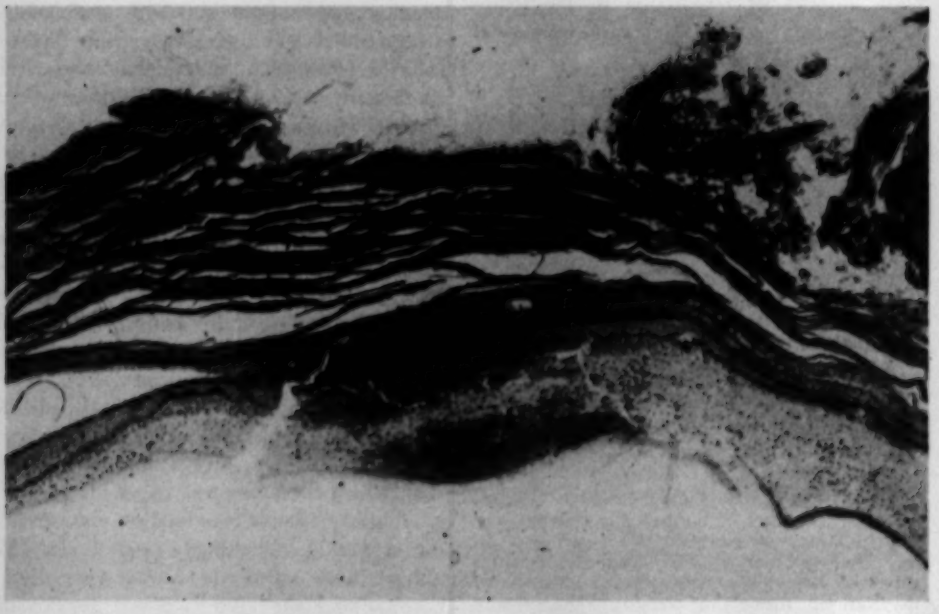

Fig. 1 (Newell, Harper, and Köistenen). Area of acute radiation injury to retina, choroid, and sclera seven days after attachment of 0.8 mc. of yttrium^{90} to the sclera. The area is necrotic and infiltrated with polymorphonuclear leukocytes which have also been necrotized by the radiation. (Hematoxylin and eosin; ×55.)

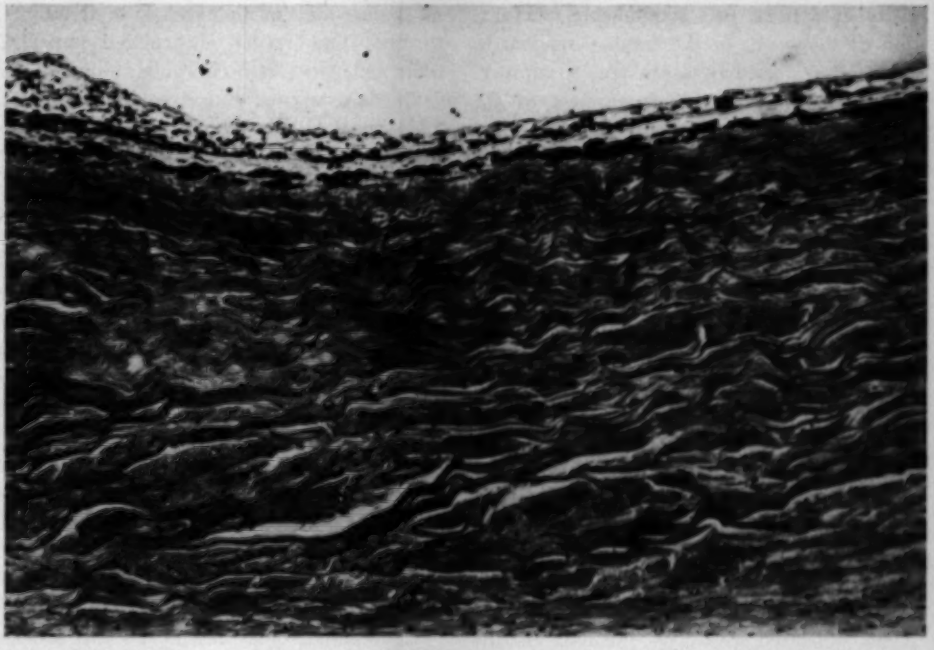

Fig. 2 (Newell, Harper, and Köistenen). Complete destruction of retina 75 days after the attachment of 0.8 mc. of yttrium^{90} to the sclera. (Hematoxylin and eosin; X120.)

which, however, was not as marked as that which occurred in the internal nuclear layer. The ganglion-cell layer, histologically at least, appeared the most resistant of retinal layers to radiation damage. Nonetheless similar changes were present as in the nuclear layers but were less marked.

The retina was entirely destroyed so that individual layers could not be recognized in an area two mm. in diameter. Injured cells were observed in an area approximately six mm. in diameter. The area of acute injury to the sclera was four mm. in diameter and necrotic cells were evident in an area eight mm. in diameter.

The application of a 0.8-mc. pellet for a seven-day period led to similar changes. By this time, however, vascular engorgement of the choroid was not marked and blood vessels were recognized only with difficulty amid the cellular debris. Many necrotic polymorphonuclear leukocytes were present in the sclera, choroid, and retina. Many cystic areas were present in the retina in adjacent areas where the choroid and sclera were relatively uninvolved. In areas adjacent to the site of most intense damage, choroidal pigment proliferation was evident and the choroidal vessels in this area were dilated.

Fourteen days after the application of a 0.8-mc. pellet the acute process was seen to be subsiding and the polymorphonuclear leukocytes in the area were not necrotic. Many macrophages were scattered through the necrotic sclera and retina. The sclera was considerably thinned and only occasional collagenous bundles were present which were not interwoven in the normal fashion. In many areas the retina was detached with a protein-rich fluid between it and the choroid. In the area of most acute inflammation the retina was entirely destroyed. In the adjacent retina, the internal nuclear layer and ganglion cell layer were the least injured; next the external nuclear layer; and most severely the layer of rods and cones. In

many eyes there was spontaneous perforation of the sclera or the trauma incident to enucleation caused an ectatic area to rupture.

The ophthalmoscopic appearance of the eyes paralleled the histologic changes. Usually the first change was hemorrhages which frequently surrounded and obscured the optic disc. Pigment proliferation was evident by the second week and by the third week was very marked. In the final stages an area of retinal and choroidal atrophy was evident, presumably in the area of the most intense irradiation, and this was surrounded by a ring of pigment. Frequently pigment proliferation was very marked.

In eyes removed 25 to 75 days after the application of comparable amounts of yttrium^{90} as in the acute studies, the histologic changes were similar. In some the sclera was ruptured and the intraocular content had escaped. The acute inflammatory reaction had entirely resolved and the adjacent areas of sclera appeared relatively normal. At the site of the most intense reaction the choroid and retina had been entirely destroyed. Adjacent to this there was an area of pigment proliferation and the gradual occurrence of normal choroid. Generally speaking, the histologic changes in the retina were more conspicuous and more widespread than changes in the choroid.

The area of complete destruction of the retina measured some five mm. in diameter. Partial destruction included an area of almost nine mm. in diameter. It is of interest to note that retinal destruction appeared more extensive than choroidal, although the retina is composed entirely of neural tissue. This resulted, probably, from damage occurring in the retina because of radiation per se, combined with damage due to interference with the choroidal blood supply. Moreover the choroid, composed essentially of vascular channels, in time regenerates in the peripheral area of radiation injury, while the retina remains unchanged.

Cataract formation was not noted in these animals either clinically, when examined with the ophthalmoscope, or histologically in serial section study. This may occur because of the relatively short time the animals were observed or because of their maturity which would make them more insensitive to radiation cataract.

Summary

Ophthalmoscopic and histologic studies were made of mature rabbits' eyes following irradiation by means of a radioactive yttrium pellet attached to the sclera. The initial reaction was one of acute necrosis in which participating polymorphonuclear cells were also destroyed. Proliferative activity was evident in the choroid after two weeks. In the area of acute injury the choroid and retina were entirely destroyed.

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THE EFFECT OF HISTAMINE ON THE RABBIT'S CORNEA*

W. G. Hagedoorn, M.D., and Elizabeth R. Maas
Amsterdam, Holland

It will be remembered that the allergic reaction is explained as a result of the union of antigen and antibodies. It is claimed that, if this union occurs in the tissue cells, histamine or histaminelike substances are liberated and cause the wheal or flare in vascular tissues.

Even though antihistamines have been developed, the problem of the etiologic significance of histamine in allergic phenomena is by no means solved. One theory is based on the fact that the symptoms of experimental anaphylactic shock are very similar, but not completely identical, to those of an adequate histamine injection. In spite of substantial criticism, histamine is accepted to be at least an important element in the mechanism of allergy, anaphylaxis, and hypersensitivity.

The role of histamine in an allergic response has further been confirmed by the fact that it is a powerful dilatator of capillaries. In the avascular tissue of the cornea allergic reactions occur. Experimental proof was given by Wessely who produced an anaphylactic keratitis in the rabbit by repeated injections of horse serum in the cornea. Experimental work was also done on the anaphylactic properties of the cornea by von Szily and Arisawa.

It seemed to us attractive to study the effect of histamine on the avascular tissue of the cornea of the rabbit. If histamine plays a role in the mechanism of the violent allergic reaction Wessely described, it might be expected that histamine will not be indifferent to the corneal tissue. We failed to find any statement in the literature on the effect of histamine on the avascular tissue.

Experiments

The following experiments were done:

Ia

In Rabbit 1, a central erosion of the corneal epithelium of about 0.5-cm. diameter was made. Cotton wool, dipped in 1:1,000 histamine-chloride, as used in provoking gastric secretion, was pressed on the defect for 60 seconds on the first day. This was repeated every 10 minutes during eight hours. On the second day histamine-chloride was applied 15 times every 10 minutes and then six times every hour, and on the third day 15 times every 30 minutes. On the second and third days, the cornea was nearly clear and the erosion still present. On the fourth day, there was slight corneal edema with some folds in Descemet's membrane. The next day the cornea was nearly clear.

Ib

The same experiment was done with physiologic salt solution as the fluid. The defect of the corneal epithelium of Rabbit 2 and the slight haziness of the stroma were only a little more pronounced in the histamine rabbit.

Comment. From this experiment, it seemed probable that histamine did not particularly irritate the corneal tissue. In another series of experiments histamine (1:1,000) was injected directly into the corneal tissue. Serial photographs were made; the first one a few minutes after the injection.

IIa

Physiologic salt solution (0.05 ml.) was injected in an area near the limbus of the left cornea of Rabbit 3. The globe was luxated in order to make clear photographs. The results showed:

9:25 A.M. Injection.

* From the Eye Hospital of the University of Amsterdam.

9:30 A.M. A milky patch in the cornea between the center and the limbus of about one sixth the size of the cornea.

9:40 A.M. The milky region is still opaque in the center and clearing up at the periphery.

10:07 A.M. The patch is small and the iris visible even through the center.

10:25 A.M. There is a very slight haziness of the whole cornea; the central part of the original patch still remains a little cloudy.

10:43 A.M. The epithelium of the cornea is still slightly irregular so that the corneal reflex is not sharply outlined. There is some haziness of the cornea.

11:00 A.M. The photograph is made with the eye in the socket again. There is still a slight irregularity of the corneal surface and slight edema and hyperemia of the bulbar conjunctiva.

11:30 A.M. Cornea and conjunctiva normal.

Comment. From this experiment it was shown that two hours after intralamellar injection of physiologic salt solution cornea and conjunctiva regain their normal aspect.

IIB

Histamine-chloride (0.05 ml.) was injected into the left cornea near the limbus of Rabbit 4. Photographs of the luxated eye showed:

9:25 A.M. Injection.

9:30 A.M. A milky patch in the cornea between the center and the limbus of about one sixth the size of the cornea.

9:45 A.M. The patch is becoming more translucent; a tiny intralamellar precipitate becomes visible.

10:05 A.M. The cornea is still more clear.

10:30 A.M. In the photograph the patch apparently is a little more opaque.

10:47 A.M. In the photograph the patch is slightly more opaque.

11:25 A.M. The patch cleared up considerably.

11:35 A.M. The eye is in the socket, the cornea is clear, the epithelium slightly ir-

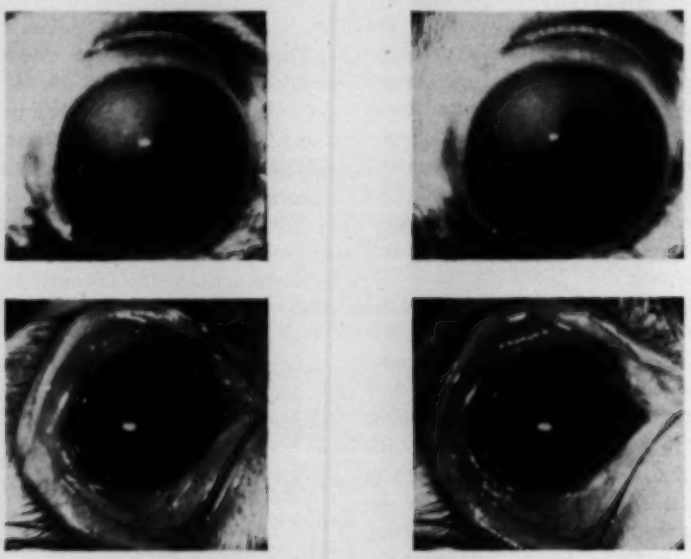

Fig. 1 (Hagedoorn and Maas). Stereophotograph of the left eye of Rabbit 4. (Above) At 9:30 a.m., five minutes after injection of 0.05 ml. histamine-chloride into the cornea. (Below) Same eye 170 minutes after the injection. The cornea is clear; the conjunctiva is chemotic.

regular. There is considerable edema and capillary dilatation of the conjunctiva.

12:15 P.M. The cornea is clear, but the inert precipitate is still there. The conjunctiva is swollen.

3:20 P.M. Conjunctival edema decreases.

Comment. Two hours after the intralamellar injection of histamine-chloride only a slight haziness and a tiny inert precipitate were left. The conjunctiva, however, was swollen, with dilatation of the blood vessels. In these rabbits the eye was luxated for every picture with the exception of the last ones. In the next experiment the eye was left in the socket.

IIc

In Rabbit 5, 0.05 ml. of physiologic salt solution was injected into the right cornea near the limbus (as in Rabbit 3). Findings were:

9:30 A.M. Injection.

9:37 A.M. The patch is less dense than in Rabbit 3.

9:47 A.M. Little change.

10:07 A.M. The patch has cleared considerably; there is slight conjunctival edema and vasodilatation.

10:12 A.M. Little change.

10:36 A.M. Conjunctival edema and vasodilatation slightly more pronounced.

10:47 A.M. The cornea is clear.

11:43 A.M. The eye is normal.

Comment. In this experiment, one hour after the injection the cornea was normal again. There was only slight edema and hyperemia of the conjunctiva.

IId

In Rabbit 6 0.05 ml. of histamine-chloride was injected intralamellarly near the limbus. The results showed:

9:30 A.M. Injection.

9:35 A.M. A dense white area is seen.

9:52 A.M. Little change.

10:05 A.M. The patch is translucent; there is conjunctival edema and capillary dilatation.

10:18 A.M. The patch is still more translucent; the conjunctiva edematous.

10:34 A.M. The cornea seems to be slightly opaque.

10:50 A.M. The cornea is clearing.

11:40 A.M. The patch is still visible; there is conjunctival edema and capillary dilatation.

12:25 P.M. The cornea is clear but there is still edema and capillary dilatation of the conjunctiva.

3:45 P.M. The conjunctiva is not yet normal.

5:45 P.M. The conjunctiva is becoming more normal.

Comment. The histamine patch was visible a little more than two hours after the injection and the irritation of the conjunctiva lasted several hours.

IIe

The photographs suggested that there might be a slightly increased cloudiness of the cornea of Rabbit 6 about one hour after the injection of histamine. This was not observed and could not be confirmed in another rabbit (7).

IIf

In Rabbit 8, 0.1 ml. of histamine-chloride was injected intralamellarly near the center of the cornea. The findings were:

11.25 A.M. Injection.

11:30 A.M. A dense white patch near the center of the cornea.

12:45 P.M. The patch is much smaller and more translucent; there is considerable conjunctival edema and capillary dilatation.

2:15 P.M. There is only a very slight opacity in the center in a completely normal cornea. The conjunctival edema has nearly disappeared; there is a slight hyperemia at the limbus.

Comment. In three hours the effect of the intralamellar injection of 0.1 ml. histamine-chloride had vanished. The conjunctival edema and capillary dilatation were negligible in the eyes injected with physiologic

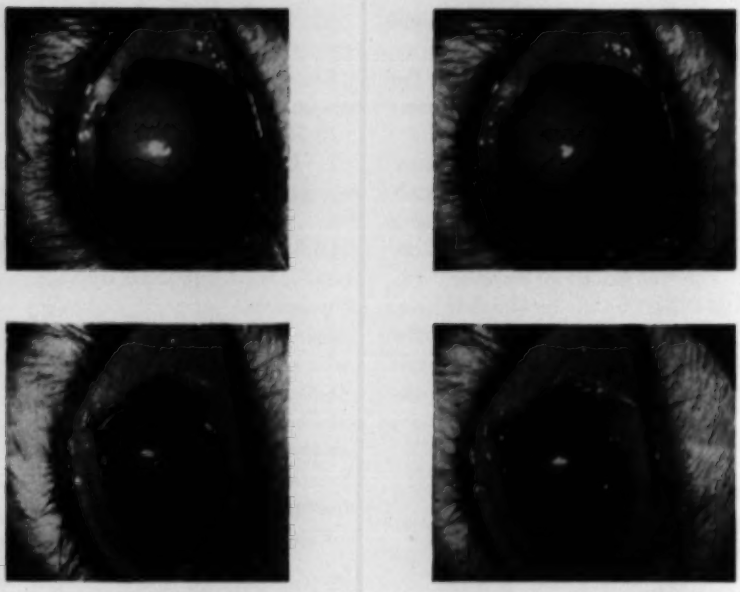

Fig. 2 (Hagedoorn and Maas). Stereophotograph of the right eye of Rabbit 8. (Above) At 11:30 a.m., five minutes after injection of 0.1 ml. histamine-chloride into the cornea. (Below) Same eye 90 minutes after injection. The cornea is clearing; the conjunctiva is chemotic.

salt solution but marked in the histamine eyes. Especially in an eye which was luxated several times for photography was there a very considerable difference from the salt-solution eye treated in the same way. Probably the exposure of the conjunctiva and the strangulation of the luxation contributed considerably to this reaction.

In the eye injected intralamellarly with 0.10 ml. histamine and which was left in the socket, the conjunctivas were hyperemic after five minutes and, after 10 minutes, chemosis developed. After 40 minutes, the limbal region especially was red and there was marked hyperemia and swelling of the conjunctivas. After two and one-half hours the palpebral conjunctiva was still swollen and hyperemic. There was some mucous secretion which contained epithelial cells and leukocytes.

It may be concluded that histamine in concentrations used to stimulate gastric secretion does not provoke a pronounced reaction in the rabbit's cornea. However, rabbits are less sensitive to histamine than other animals (Rose). Recently it has been established that a histamine injection directly into the gastric arteries is not followed by gastric secretion. However, if histamine has been mixed with blood for some time the classic response of gastric secretion appears. This fact suggests that not histamine itself but a more complex compound of histamine may be active (Born and Vane).

IIIa

The following experiments were carried out:

1. Rabbit 9 was injected intralamellarly with 0.1 ml. of the mixture of 0.15 ml. histamine-chloride and 1.0 ml. blood serum.

2. Rabbit 10, the same but with blood instead of serum.

3. In Rabbit 11, we used 0.05 ml. of a mixture of 0.1 ml. histamine-chloride and 1.0 ml blood.

4. The same was done to Rabbit 12.

5. In Rabbit 13, we used both eyes, in-

jecting 0.05 ml. of a mixture of 0.1 ml. salt solution and 1.0 ml. blood.

Although in all except Rabbit 9 (1), a bloody cornea developed, there was no such reaction as might be expected upon injecting a drug which is supposed to have an irritating effect on the corneal tissue. The cornea injected with the mixture of serum and histamine did not differ in appearance from the cornea in rabbits injected with physiologic salt solution or pure histamine. Similar experiments were carried out with acetylcholine (100 mg./1.0 cc.) with equally negative results.

Conclusion

The injection of histamine or acetylcholine in the rabbit's cornea does not provoke any notable response of the corneal tissue. Histamine mixed with blood or serum and injected into the rabbit's cornea has no effect which suggests that the "histamine compound" active in gastric secretion is an active agent in an allergic response of the corneal tissue. The substances appearing by the union of antigen and antibody in allergic reactions of the cornea cannot be identical with histamine or histaminelike substances.

Wilhelmina-Gasthuis.

Acknowledgment

We are most grateful to Mr. A. J. J. Lammens for making the photographs and for further technical assistance.

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ABSENCE OF THE MEDIAL RECTUS*

Its successful treatment by vertical tendon transplants

Howard F. Hill, M.D.
Waterville, Maine

The following case is presented because search of the literature has failed to disclose any report of successful transplantation in the human eye of the superior and inferior rectus tendons nasally, for correction of complete and irreparable loss of function of the medial rectus.

Literature

In 1907, Hummelsheim[1] was the first to work experimentally on monkeys' eyes, solely to test the effectiveness of a surgical procedure by removing the anterior portion of the medial rectus and transplanting portions of the superior and inferior recti nasally to the medial rectus stump. A year later, Hummelsheim[2] reported transplanting portions of the vertical tendons laterally in the human eye for paralysis of the lateral rectus. His method, plus many modifications, has been reported in the literature in cases of sixth-nerve paralysis, with results that have differed markedly.

Some authors, including Scobee,[3] have felt that little more was gained by this technique than by surgery of the horizontal muscles alone. Scobee stressed that many of these operations on the horizontal muscles produce useful abduction, and if the Hummelsheim procedure is to be carried out, it should be done in two stages with interval enough between to evaluate the results on the horizontal muscles alone. I have carried out this two-stage technique in a case of congenital sixth-nerve paralysis, and obtained abduc-

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tion only after the second procedure on the vertical muscles was performed.

The experimental work on Rhesus monkeys by Marina, Olmsted, Margutti, and Yanageaswa, and Leinfelder and Black is reviewed in Chamberlain's[4] recent studies on the extraocular muscles in monkeys. Chamberlain concluded from his work that the superior and inferior recti do act as secondary adductors in monkeys' eyes.

Verhoeff[5] has refuted many of the conclusions drawn from the work done on monkeys' eyes. He[6] also feels that the results reported from these experiments cannot be applied to human eyes.

Adler[7] states that contraction of the superior and inferior recti produces adduction when the eye is in primary position, and becomes increasingly effective as the eye is inwardly rotated. The concept that the superior and inferior recti act as secondary adductors is supported by several authors, including Jackson,[8] Duane,[9] Peter,[10] Scobee,[3] and Fink.[11]

O'Connor[12] tried a full vertical tendon transplant for the correction of a lateral rectus palsy but found it resulted in profound vertical muscle imbalance.

The Hummelsheim technique used for sixth-nerve paralysis has been adequately reviewed by Langdon and his associates,[13] and later by Berens and Girard.[14]

Berens[15] has used this technique for loss of function of the medial rectus, but the results have not been reported. McLean[16] has transplanted the split tendons of the inferior and superior recti nasally in one case, and Fink[17] has used this procedure; however, their results have not been reported.

Stallard[18] and Peter[10] both mention that paralysis of the internal rectus may be treated by surgical transplantation of the vertical recti, but no cases are cited.

Case report

On February 8, 1954, a white woman, aged 33 years, was seen complaining of diplopia of four years' duration. She carried her head habitually turned to the left, and by an extreme left position was able to avoid diplopia. The right eye was exotropic. She stated that four years previously, while living in New Jersey, she had had a tumor mass removed from the inner canthus of the right eye. Following surgery, the right eye remained turned out in the present position. Since the operation, she had carried her head in the extreme left position and become very self-conscious due to the cosmetic effect. She was able to read by covering one eye.

Examination disclosed the right eye to be fully exotropic and with no power of adduction. There was an elevated, fixed tissue mass one centimeter in diameter in the inner canthus. Her visual acuity was 20/20 in each eye, and there was binocular fixation with the head turned to the left. The ocular motility of the left eye was normal. With the head straight, the right eye remained fully exotropic. With the left eye covered, there was no adduction, but, on attempting to adduct, there was a slight, jerky, up-and-down motion. Vertical movements were normal, except as modified by the absence of any action of the medial rectus.

Her former ophthalmologist reported that a tumor which extended underneath the medial rectus had been removed from the inner canthus. The pathologic report from the Armed Forces Institute of Pathology was:

"The sections are of a mass of fat and dense collagenous connective tissue. Epithelium, hair follicles, and sebaceous glands are not included in the sections submitted. In the absence of these, the tumor must be classed as a lipoma with larger than usual amount of collagenous stroma. There is no evidence of malignancy."

Surgery was advised and and accepted.

Operation

Under sodium pentothal anesthesia, the following procedure was carried out. The conjunctiva was dissected free of the mass in the inner canthus. This tumorlike mass

was cautiously dissected out, and an attempt was made to locate the medial rectus. The former insertion of the tendon was visualized, but careful dissection deep into the orbit failed to locate any portion of the muscle. Tenon's capsule could not be identified in this area.

The tumor mass was sent to the pathologic laboratory and reported as "Granulation tissue infiltrated with lymphocytes. The appearance of the tissue is not characteristic of any specific neoplastic process. Interspersed in some areas, are groups of skeletal muscle fibers."

The lateral rectus was recessed five mm. The superior rectus was then exposed and divided with as little trauma to the capsule as possible. The medial half of the tendon was transplanted to the former insertion of the medial rectus. The remaining portion of the superior rectus tendon was moved nasally four mm. beyond the nasal border of the superior rectus insertion, and sutured in place.

The same procedure was carried out upon the inferior rectus tendon. Care was taken not to traumatize the oblique muscle tendons. Chromic 6-0 sutures were used in the transplantation, and 6-0 silk running untied sutures were used to close the conjunctiva. Binocular dressings were applied.

Postoperative observations

Due to the trauma of such extensive surgery, particularly in the area of the medial rectus, there was considerable edema and reaction for several days. At the end of three days, the eyes were straight but with no adduction present. At the end of two weeks, the patient had slight adduction over the midline. At four weeks, the right eye had developed adduction of 23 degrees. There was no diplopia up to this point, and the patient held her head in a normal, straight position. She had binocular fixation, and could read comfortably.

On extreme upward gaze, the right eye diverged and diplopia was present. There was diplopia in extreme downward gaze due to the slight limitation of downward motion of the operated eye.

The patient apparently had a convergence amplitude of 14 prism diopters and a divergence amplitude of 14 prism diopters. Stimulation of the convergence mechanism, by having the patient fixate upon a near object, produced 12 degrees of adduction in each eye. With the operated eye covered, fixation upon a near object caused the covered eye to turn in.

As convergence is a function only of the horizontal recti, the convergence mechanism probably induced convergence in the unoperated eye, plus relaxation of the lateral rectus in the operated eye. It was felt that the adduction of the operated eye must in some way be activated by the convergence mechanism, as the eye turned in when covered and convergence was stimulated. As suggested by Verhoeff[10] the question arises as to whether or not there is still some power in the medial rectus of the operated eye, although a careful search deep into the orbit failed to disclose any portion of the stump.

Comment

Search of the literature failed to disclose a report of successful transplantation of the inferior and superior recti nasally in the human eye for loss of function of the medial rectus. It was felt that with a patient who had an isolated and permanent loss of action of a medial rectus, the Hummelsheim technique or, better, one of its modifications would be a logical procedure. As it is generally stated that the superior and inferior recti act as secondary adductors, it seemed more logical to use these tendons to replace an active medial rectus than to use these same tendons to replace loss of function of the lateral rectus. Points in favor of this procedure are:

First, the transplanted tendons would have the same innervation as that of the replaced medial rectus.

Second, there would be the synergistic ac-

tion that the superior and inferior recti are thought to have as secondary adductors.

Third, this secondary adduction could be enhanced by moving the remaining portions of the split tendons, that is the lateral halves, nasally beyond the original stumps of the vertical insertions. This modification of the Hummelsheim technique was suggested to me by McLean,[16] and may well be a most important factor in producing adduction.

Fink,[17] although recognizing the advantage in displacing the lateral portions of the vertical tendons nasally beyond the original insertions, has hesitated to do so because of the possibility of disrupting the vertical gaze.

Verhoeff[19] feels that splitting of the tendons is not logical and advocates displacement of the complete vertical tendons nasally and their resection. Against the Hummelsheim technique of tendon splitting are the trauma involved and the weakening effect on the vertical action. In Chamberlain's[4] work on monkeys' eyes, the post-mortem studies showed the value of avoiding trauma by careful dissection. With split tendons that were carefully dissected, particularly in regard to the capsule, no extensive adhesion to the sclera occurred.

In favor of splitting of the tendons is the fact that all the recti muscles are much more powerful than their function ordinarily requires, probably offsetting any weakening effect on the muscles involved.

As suggested by Cogan,[20] the evidence in favor of the superior and inferior recti acting as adductors would have been more conclusive if the recession of the lateral rectus had been postponed to a later date.

From a clinical viewpoint, the lateral rectus in this patient had undergone considerable secondary contraction, and it was felt that a recession was necessary to obtain adduction.

Summary

A case of complete and irreparable loss of function of the medial rectus of the right eye presented an unusual opportunity to evaluate the effect of transplanting portions of the superior and inferior recti nasally.

This patient obtained fair inward motion of the affected eye, was relieved of an embarrassing cosmetic disfigurement, and has obtained useful binocular vision.

33 College Avenue.

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CLINICAL PATHOLOGIC CONFERENCE*

LORENZ E. ZIMMERMAN,† M.D.
AND
L. CONNOR MOSS,‡ M.D.
Washington, D.C.

CASE HISTORY

An 80-year-old woman complained of frontal headaches associated with severe pain in the right eye.

Present illness. Three weeks prior to enucleation, the patient experienced sudden onset of frontal headaches associated with severe pain in the right eye. The right eye burned, itched, and became bloodshot. The severe headaches and the right-eye pain were associated with nausea and vomiting but no vertigo. The right eyelid became markedly swollen.

Past history. Twelve years earlier the patient had had a cataract extraction on the left side. The patient stated that her right eye had been blind for the past 10 years although she did not know the cause of blindness.

Physical examination. There was moderate palpebral edema of the right eyelid and the eye was markedly congested. The right cornea was diffusely cloudy. The anterior chamber was deep and contained a mass which, on first examination, was thought to be an anterior dislocation of the lens. Subsequent examination led to the belief that this was a mass of exudate, having a grayish white color. The right iris appeared deeply congested, presented an unusual color, and was not seen clearly. The pupil appeared irregularly dilated and could not be visualized clearly because of the exudate in the anterior chamber. The lens appeared cataractous and because of this the right fundus could not be visualized. No fundus reflex was obtained.

Examination of the aphakic left eye revealed a surgical iridectomy with coloboma from the 11- to 1-o'clock position. A thin secondary membrane was present but there was a good central opening. There was evidence of old inactive choroiditis juxtapapillaris and moderate retinal arteriolar sclerosis. Tension was: O.D., 90 mm. Hg with the McLean tonometer when first seen; two days later it had gone down to 60 mm. Hg. Blood pressure was 170/110 mm. Hg. Serologic tests for syphilis were negative, as was the urinalysis.

Course. Enucleation was advised when the patient was first seen but she refused. Treatment consisted of two-percent pilocarpine drops and eserine ointment. There was temporary symptomatic relief in that the severe headaches, right-eye pain, nausea, and vomiting all decreased in severity and the tension dropped from 90 to 60 mm. Hg. There was recurrence of the ocular pain, frontal headaches, nausea, and vomiting and the patient submitted to enucleation.

DIFFERENTIAL DIAGNOSIS

Dr. Moss: The chief complaint, history of the present illness, external examination and tonometric readings, give us the diagnosis of acute congestive glaucoma in the right eye.

The presence of a cataract in the right eye, this eye having been blind for 10 years, and a cataract had been removed from the left eye 12 years previously, points to the probability of the cataract in the right eye as being hypermature. Blindness suggests that the lens has been densely opaque and that

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* From the Registry of Ophthalmic Pathology (AFIP Accession No. 615365). Presented during the Postgraduate Course in Ophthalmology conducted by Col. John H. King at Walter Reed Army Hospital, February 2, 1955.

† Chief, Ophthalmic Pathology Section and Registrar, Registry of Ophthalmic Pathology, Armed Forces Institute of Pathology.

‡ Surgeon, Episcopal Eye, Ear, and Throat Hospital; Consultant in Ophthalmology, Walter Reed Army Hospital.

10 years is adequate time for degeneration of the lens to have taken place.

It is borne in mind that some serious pathologic change other than cataract could have taken place in the right eye as, for example, a long-standing, damaging glaucoma, or a venous thrombosis, leaving the eye without light perception. At least, an additional pathologic process does not seem essential to the acute episode which occurred.

It is stated that a secondary membrane was present in the left aphakic eye. This leads one to believe that an extracapsular extraction was done which necessarily leaves a variable amount of lens cortex to be absorbed. Hemorrhage following an intracapsular extraction can leave a pupillary membrane, but it would be likely to have a uniform density and not show a clear central opening. There is the theoretic possibility that, following the absorption of the remaining lens cortex, a sensitivity to lens protein developed; the stage then being set for a particularly violent reaction if ever lens material were liberated into the other eye.

The diffusely cloudly cornea would be present in acute glaucoma, and especially so, if the lens nucleus should have escaped from the capsule and come to rest against the posterior surface of the cornea. The deep anterior chamber and the absence of a widely dilated pupil rule out an intumescent cataract. The receded iris and deep anterior chamber are characteristic of a shrunken, degenerated lens. Rupture of the posterior lens capsule does not set up the violent reaction that takes place when the anterior lens capsule ruptures. Acute congestive glaucoma commonly occurs when the anterior lens capsule ruptures and allows the escape of lens material into the aqueous.

In the picture presented, it is presumptive that a rupture of the anterior capsule took place. Following the rupture of the capsule, the lens nucleus could have escaped into the anterior chamber, become surrounded by exudate and be identified as a "grayish white mass." The iris not being clearly seen, can be explained by the hazy cornea and an aqueous clouded with exudate and lens debris, or, perhaps, even cholesterol crystals in addition. The deeply congested iris and "unusual color" make one wonder as to the possibility of rubeosis iridis. Certainly without rubeosis, there would seem sufficient reason for the iris to have an "unusual color."

Last, we must remember that a certain appreciable percentage of blind eyes harbor malignant tumors, which, if present in this instance, could highly modify the entire concept we regard as probable.

Let's have some of the diagnoses submitted by you and let's hear you defend or justify them.

Diagnoses

Dr. Zimmerman: We received diagnoses from 35 persons. There were 12 diagnoses of glaucoma secondary to hypermature cataract and one person suggested glaucoma secondary to exfoliated lens capsule. Others considered glaucoma secondary to uveitis (seven), sympathetic uveitis (three), and vascular occlusion (four). There were four votes for phacoanaphylaxis, and single suggestions of tumor, panophthalmitis, and tuberculous endophthalmitis.

Dr. Moss: I am a little surprised that three of the diagnoses go back to sympathetic uveitis. Certainly there is very little said about the aphakic eye showing any inflammation whatsoever. Of course the possibility of venous occlusion and rubeosis was mentioned. I don't think the findings in the aphakic eye with the choroiditis juxtapapillaris and the sclerosis have any necessary bearing at all on the situation in the cataractous eye. I do think that, even without rupture of the capsule, it is possible to excite an exudate in the anterior chamber which was identified as a grayish white mass. But certainly it seemed to show the violent picture of rupture of the capsule. I only mentioned the possibility of phacoanaphylaxis in that we have the ideal setup for the development of such. It had been 12

years since cataract extraction—presumed to have been extracapsular—12 years for the development of sensitivity and hence phacoanaphylaxis. But it is not essential in this case, because lens material could escape into the anterior chamber even without this additional factor of phacoanaphylaxis. Any questions?

Question: With phacoanaphylaxis as a factor would not there be a more violent reaction than just mere leakage such as we see over a long time in many hypermature lenses with mild irritation?

Dr. Moss: Mild irritation is possible, as we mentioned—a long-standing glaucoma without the symptoms which occur with acute congestion. Certainly there apparently was nothing prior to the acute onset that called the attention of this patient to the eye. She lived with this blind eye comfortably for 10 years. It was quiet until the storm of the acute glaucoma. Questions?

Question: What about severe intraocular hemorrhage?

Dr. Moss: Severe intraocular hemorrhage is quite possible but certainly there is no description of it in the anterior segment of the eye. There could be severe hemorrhage but I don't believe a severe intraocular hemorrhage would precipitate such an affair as this—such an acute affair. We tried to stick to the description presented to us. We knew that there were certain things that Dr. Zimmerman was holding out, but we did our best with the data furnished. We didn't try to read more into it than was presented to us, although our speculation went riot at times! Is there any further discussion?

Pathology

Dr. Zimmerman: Let's have the first slide, please. You will note as was described clinically the anterior chamber is deep (fig. 1). You will also note that there is definite evidence of glaucoma here, a cupped disc. In spite of this there are no synechias, either anteriorly or posteriorly. Let's look at the next section at higher power (fig. 2). This

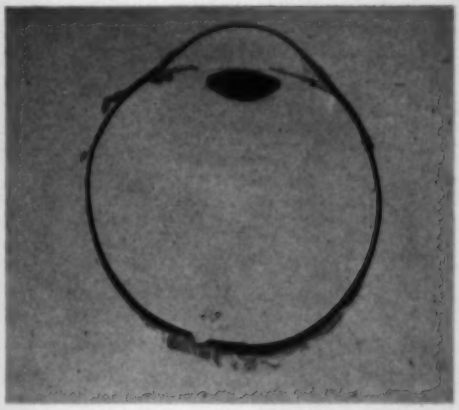

Fig. 1 (Zimmerman and Moss). Hypermature cortical cataract and phacolytic glaucoma. The disc is cupped and there is atrophy of all coats at the equator. In spite of glaucoma there are no synechias and the anterior chamber is deep. Only the sclerotic lens is seen clearly at this magnification (×2).

is just the lens nucleus, but I can't prove it to you until we see the next section, please. Here you will see the anterior lens capsule, the posterior lens capsule; in fact the capsule is intact all the way around (fig. 3). This is the sclerotic lens nucleus.

The remainder of the lens, the lens cortex, is completely liquefied. With that liquefaction, fluid lens material has escaped and the capsule has collapsed. Here the anterior and posterior capsules are almost in apposition. This liquefied cortical material has the ability to escape through the more permeable, though still intact, lens capsule, as Dr. Moss indicated. And when it does this, it excites a histiocytic cellular response—these large mononuclear cells come into the aqueous—here you can see some along the posterior capsule—here a little on the anterior—here a portion of that mass that was described clinically (fig. 4).

Let's look at the next section. Here is the equatorial region of the lens under higher power. Perhaps you can see this pale material in the anterior chamber which represents the liquefied cortical material, and here is some of this mononuclear cellular reaction on the outside of the lens capsule pos-

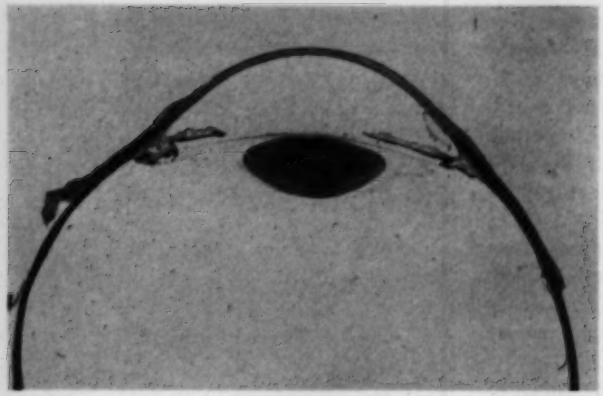

Fig. 2 (Zimmerman and Moss). Anterior segment magnified ×6. The anterior and posterior lens capsules are in close apposition as a result of marked loss of liquefied cortical material.

teriorly, and the same thing here anteriorly (fig. 3).

Notice that within its capsule the lens is completely devoid of cells. We take this as evidence that the lens capsule has not ruptured and that this seepage of liquefied cortical material has been from within outward, and the cells have not come in. Most of the material that was described clinically in the anterior chamber has fallen out during processing but we see a portion of it left here in the chamber angle (figs. 3 and 4). Note again that the angles are open—there are no synechias—no posterior synechias either. Next slide please.

Here is this material on the anterior lens capsule under somewhat greater magnification, and you can begin to see some of the characteristics of these cells. They are very typical—those cells that have picked up the liquefied cortical material swell up and become rounded. Their cytoplasm is distended with finely granular degenerated lens material. This material is carried into the anterior chamber (figs. 4 and 5). Here we see these cells that I have just described to you, and this I am quite convinced is the massive exudate that was described clinically and which temporarily was thought to be a dislocated lens.

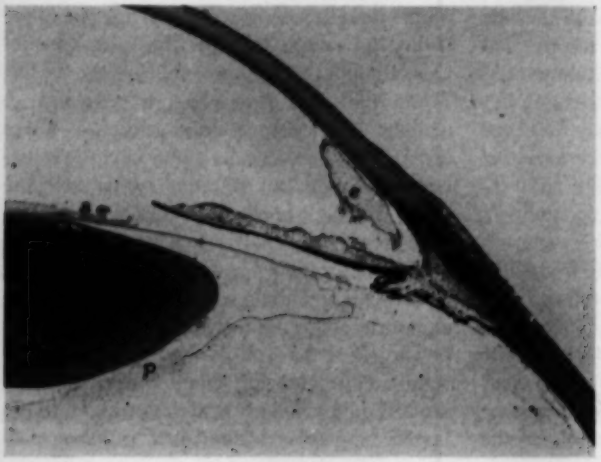

Fig. 3 (Zimmerman and Moss). Complete liquefaction of lens cortex with partial collapse of capsule. Evidence of capsular rupture is lacking. Although dense accumulations of macrophages are seen on the lens surface anteriorly (a) and posteriorly (p), there are no cells inside the lens capsule. A portion of the massive exudate in the anterior chamber that was such a striking clinical observation remains in the open chamber angle (e) (×16).

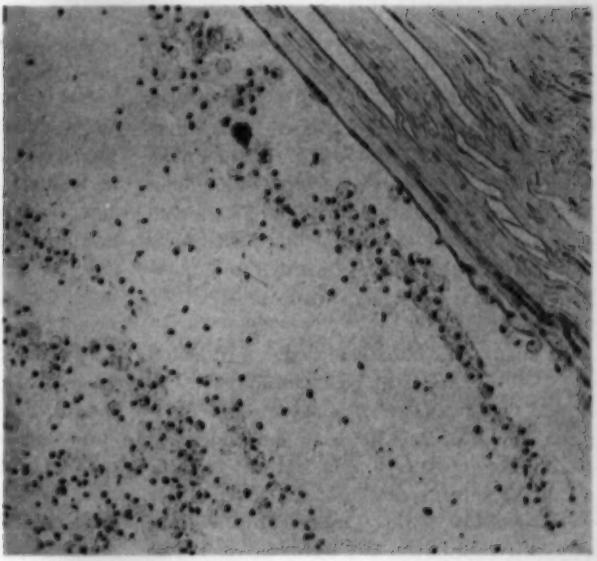

Fig. 4 (Zimmerman and Moss). The characteristic macrophagic response to hypermature lens substance is seen in this view of the anterior chamber exudate (×75).

Now for the importance of this from the standpoint of the eye as a whole. In the next slide (fig. 5), it will be seen that these cells plug the intertrabecular spaces and, by so doing, prevent the adequate escape of aqueous, thus producing a type of secondary glaucoma.

This condition, we believe, is probably a good bit more frequent than is generally appreciated, although in talking with doctors from various parts of the country, it seems that in some areas there is a high degree of awareness of this condition, whereas in other parts there is a low incidence of awareness. At any rate, the majority of cases of this type that are received by the Registry are not correctly diagnosed preoperatively. As a matter of fact we believe that, if the correct diagnosis is made preoperatively, the operation of choice is or should be lens ex-

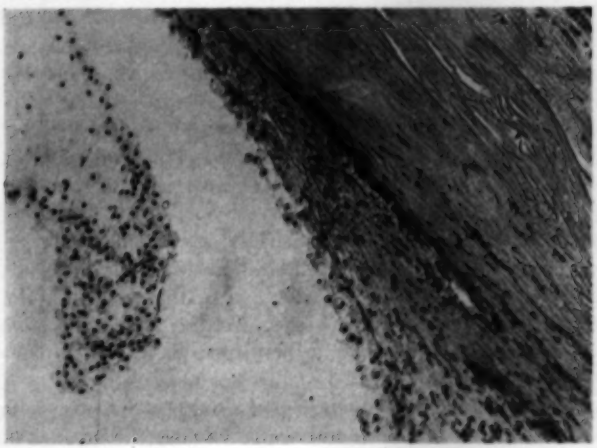

Fig. 5 (Zimmerman and Moss). Macrophages engorged with hypermature lens material cling to the endothelial surface of the cornea and corneoscleral trabeculae. This interferes with aqueous outflow and is interpreted as the usual cause of glaucoma associated with hypermature cataracts.

traction. I think there ought to be some discussion on that point in just a moment.

The material in the Registry, which now amounts to about 140 cases, was reviewed recently by Dr. Milton Flocks, Dr. Stuart Littwin and me.[1] We found that the true nature of this type of glaucoma was seldom appreciated by the attending ophthalmologist. For this reason we have coined the term **"phacolytic glaucoma"** in order to emphasize the basic pathologic process—lysis of lens material.

In many of these cases, the retina and optic nerve are still well preserved. The typical picture is that of acute onset of glaucoma in a patient who is in the middle or older age group. As a matter of fact, in about 70 percent of our cases the patients were aged 70 years or more. This woman, you will recall, was 80 years of age. The typical picture, then, is the acute onset of unilateral glaucoma in an elderly individual. In 90 percent of the cases, the other eye is either aphakic or has a cataract. That syndrome should make you immediately think of this condition, particularly if on physical examination you find that there is a deep anterior chamber, and no synechias either anteriorly or posteriorly. This, in my experience, is by far the most frequently encountered condition in enucleated glaucomatous eyes which have open angles, a deep chamber, and no posterior synechias.

The next slides will show you the retina, not from this patient, but from some of the other cases in this series where the retina is well preserved. In the present case the optic nervehead was cupped and the retina was atrophic but, in a number of the cases, there is no cupping and the nerve-fiber and ganglion-cell layers of the retina are well preserved, as is the retinal architecture in general. We think that, in such cases, removal of the lens followed by irrigation of the anterior chamber probably would provide a useful eye. This point was emphasized by the Irvines[2] who reported several cases with excellent vision postoperatively. Dr. Moss would you like to talk about the therapeutic aspects?

Discussion

Dr. Moss: Yes, after seeing the microscopic sections, this case seems an ideal one in which to relieve the acute situation with a paracentesis, or even with a syringe and needle, to withdraw the toxic material in the anterior chamber that is exciting the reaction; the way to relieve the condition is by prompt removal of the exciting material. The secondary aqueous would not contain as much toxic material. Subsequently the lens should be removed. It seems to me that the eye could be calmed down and perhaps the tension brought to normal simply by irrigation, or by any method that would change the aqueous or flush it out or allow the toxic material to escape and permit the secondary aqueous to form. It's a more simple matter since the capsule was not actually ruptured, which I thought it to be from the description.

Dr. Zimmerman: I meant to mention that, in the majority of cases, there is no evidence of capsular rupture. We believe that usually this material escapes through the degenerated but intact capsule.

A physisian: Dr. Moss suggested paracentesis; I once saw a well-known surgeon do a paracentesis of the anterior lens capsule with an ordinary needle to suck out the hypermature fluid. There should not be any fear to penetrate the capsule since it is lax anyhow.

Dr. Moss: Sounds quite reasonable because you are removing liquefied material, even if you go beyond the anterior chamber. Of course you have the subsequent problem of the nucleus which must be removed, especially after you have opened the lens capsule —you don't have a period of grace there. I had in mind to control the acute congestive glaucoma and then subsequently make plans for removal of the lens nucleus.

Dr. Zimmerman: Another difficulty with that procedure would be that, in a number of

these cases, there is practically nothing left of the cortex. That is, the anterior and posterior capsules in the equatorial region are in apposition. The little bit of cortical material that is still present clings to the nucleus or to the posterior capsule. Are there others that have had experience with this condition and its handling?

A physician: We decompressed the chamber very slowly and had no trouble with the glaucoma. Just went right in and took the lens out and that's it!

Question: Did you grasp it with a capsule forceps?

Answer: Yes, but it broke.

Question: Then you got the nucleus out by expression and then flushed it out with the anterior-chamber irrigator?

Answer: That's right.

Question: How high was the tension at the time of operation?

Answer: The tension was about 60 mm. Hg.

Question: No untoward results—you used the suture too in the usual manner? Iridectomy?

Answer: That's right.

A physician: There is one point I would like to make. If a paracentesis is done for the control of the secondary glaucoma, I think it would be well to inject air at the time of paracentesis as was pointed out by Dr. Friedenwald in his recent Schoenberg Lecture[3]—paracentesis for all secondary glaucoma. He feels that air should be injected at the time for two reasons. First, there is an immediate restoration of the anterior chamber which will decrease the incidence of peripheral anterior synechias. The second point is that the presence of gas in the anterior chamber serves as a cushion for a subsequent rise in intraocular pressure, which does occur following a paracentesis, so that if this procedure is contemplated—or a paracentesis for the control of a secondary glaucoma—I think it is well to inject air into the anterior chamber at the time.

Dr. Moss: I think that is very interesting and a well-taken point.

A physician: I had a similar case, and the woman, who was 82 or 83 years of age, did not have any light perception when she first came in. She had a hypermature cataract and all the symptoms which were mentioned here. It seemed as if we would have to enucleate but she refused flatly and we carried her along for a few days with pilocarpine and hot fomentations. The tension was in the neighborhood of 70 or 75 mm. Hg—something like that—it looked very bad. But she was a very plucky woman and she insisted that I take the cataract out, even if she wouldn't see. I told her that she might not see, and we took the cataract out and she now has vision of 20/40 or in the neighborhood of that. I had seen similar cases where light perception was absent in a hemorrhage, so in hemorrhages and, seemingly, in some cases of hypermature cataract, the lack of light perception is not all conclusive.

Dr. Zimmerman: I'm awfully glad you mentioned that, because Dr. Flocks in going over our cases was very much impressed by the fact that so often the history has indicated that the patient had no light perception, and yet when we look at the sections, the retina and optic nerve just don't look that bad. In fact we are often unable to say there is any significant change in the retina or nerve. I'm very glad to hear you say that!

Question: What is the position of the filtration angle? We notice from the slide that the angle is closed in this enucleated eye, or rather plugged. If you remove the lens, what is the expected result? Will that filtration angle reassume its normal function or will it be a glaucoma, open-angle type?

Dr. Zimmerman: The Irvines[2] reported three patients who had normal tension and 20/20 vision and a fourth patient with normal tension and 20/50 vision following lens extraction. It is possible, however, that, if the chamber is not irrigated after lens extraction, enough exudate will remain to

embarrass the outflow of aqueous.

Question: Would the use of Diamox be considered in helping control this tension prior to surgery?

Dr. Moss: I'd probably try it—there would be no harm in it. Anything you can do to reduce the tension for the immediate relief of a patient in as much distress as this one was is indicated

A physician: We had a case not long ago treated with Diamox and it is interesting that the tension was lowered in 24 hours. Then we went ahead and did an intracapsular extraction through a round pupil and the only complication that occurred was that the Diamox dropped the tension down so much that we thought it helped produce a choroidal detachment. We stopped the Diamox and tension went back to normal, so I think that Diamox is certainly a big help in these cases.

Question: Was yours a case of intumescent lens?

Answer: No! It was a hypermature cataract.

Dr. Zimmerman: In closing I wish to emphasize that this is a preventable, as well as a curable, type of glaucoma. If lenses were always removed before they became hypermature, we would never see this type of glaucoma. If treatment always consisted of lens extraction, we would not see most of the globes for the eyes would be saved.

Armed Forces Institute of Pathology.

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TARSECTOMY

J. GLIKSON, M.D.
Haifa, Israel

On the basis of more than 30 years' personal experience in operations for trachomatous trichiasis and entropion of the upper and lower lids, I agree completely with Kuhnt's method of the excision of the tarsal plate, mentioned by Meller:[1]

"It can only be applied during the scar stage of the trachoma, as the conjunctival surface can only then be easily pealed away from the shrunken tarsus."

Boase[2] writes:

"Trichiasis-entropion is the usual reason for the operation but in my experience there is no more economical way of dealing with bad cases than by tarsectomy. Progress of pannus is arrested and in most cases is followed by appreciable regression. Moderate degrees of ptosis, congenital or otherwise, can be improved by tarsectomy. This simple operation gives the highest economic return in a country where trachoma takes so heavy a toll of efficiency, for the majority of those benefited would otherwise be doomed to near-blindness."

It is my opinion that it is the lack of fresh green fodder during the seven months' dry spell in this country which is the main cause of the frequent conjunctivitis, which after years forms trachoma.[3]

Taborisky determined that thickening of the tarsus may occur in cases of chronic inflammation as late as four or five years after infection.[4]

During the first two years of my practice

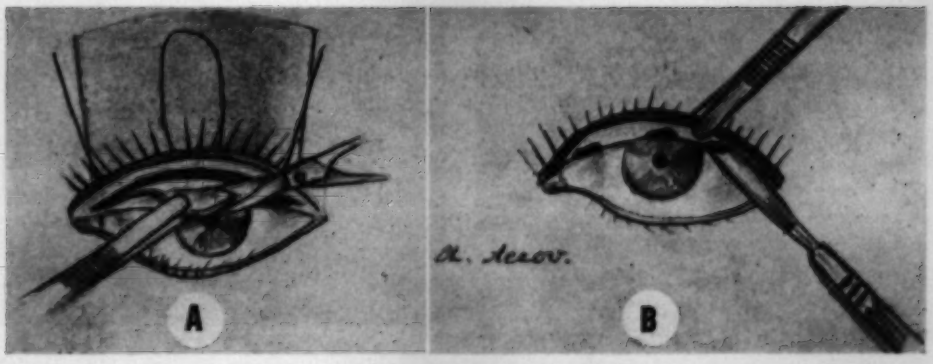

Fig. 1 (Glikson). Technique of operation. (A) Cutting of the tarsus. (B) Cuneiform cuts in the remaining tarsus.

here in Haifa, I performed a plastic operation after van Millingen. Unfortunately I often saw recurrences and it frequently happened that the malady of the tarsus and conjunctiva was transferred onto van Millingen's mucous-membrane graft.[5] After much consideration, I then tried a modified Kuhnt operation.

Before operative measures are undertaken, a novocaine injection is given externally between the skin and the tarsus, three mm. from the lashes, and internally on the medial and lateral sides of the fornix. As soon as the injection begins to take effect, a suture of four stitches is made with silk (0) two mm. from the lashes. The broad spatula plate is then placed on the skin, and the upper lid is everted by means of the sutures. The spatula and the silk sutures are held by the assistant.

An incision is then made in the conjunctiva, 1.5 to 2.0 mm. from the edge of the lid, after which it is pealed from the tarsus. The thus exposed tarsus is cut through at 1.5 to 2.0 mm. from the edge of the lid, excised from the orbicularis muscle, and cut off with curved scissors. The tarsus is seen to be distorted by fibrosis; the Meibomian glands are found to be obliterated.

The remaining edge, with the lashes on it, is everted with a strong pair of tweezers. Three, four, sometimes five cuneiform cuts are made, 1.5 to 3-mm. broad but not deeper than one third of the remaining tarsus, as atrophy of the edge and lashes could occur (fig. 1). In this way a new marginal border of 1.0 to 1.5 mm. is formed. All the lashes

Fig. 2 (Glikson). K. K., a man, aged 45 years, with trichiasis. Operation on the right upper lid on July 10, 1955. Photograph taken the day after operation following removal of sutures. No hairs are visible on the upper eyelid.

Fig. 3 (Glikson). Same patient as in Figure 2 five weeks after operation. Some small hairs are now visible. These will increase with time.

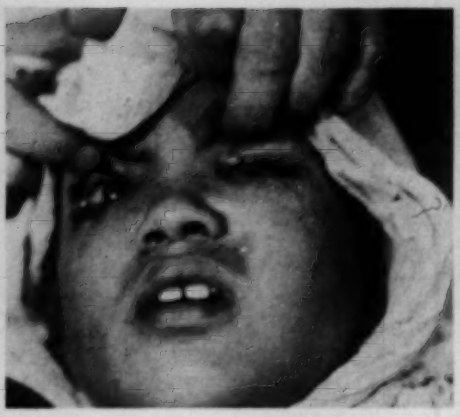

Fig. 4 (Glikson). T. K., a boy, aged nine years, with trichiasis of both lids. Eczematous keratitis is present in both eyes. On July 10, 1955, the operation was performed on both lids of both eyes. The photograph was taken the following day, after removal of the sutures. Lashes are present on all eyelids.

which previously were inside now appear perfectly normal on the outside, although previously many underdeveloped hairs grew inside.

Now, one suture is made with two needles, one laterally and the other medially. The sutures join the conjunctiva with the remaining tarsus. Both threads are tied, 0.5 mm. above the lashes.

The eyes are kept bandaged for 24 hours; the sutures are removed after 24 hours. If there is heavy bleeding, the blood vessels are cauterized; in these cases, which are extremely rare, the sutures are removed after 48 hours.

The whole operation takes seven to 10 minutes.

Fig. 5 (Glikson). Same patient as in Figure 4. Five weeks after operation. The trichiasis and keratitis have disappeared and all the eyelids are normal.

In operations of the underlid in entropion and trichiasis, as well as in the most serious trachomatous cases, the injection is made 0.5 mm. below the lashes, and a few drops of Pantocaine are dropped into the eye. The spatula is then introduced into the lower fornix and the skin and muscles are cut 0.2 mm. below the lashes. A second, parallel cut is then made with a scalpel, approximately 1.0 to 1.5 mm. beneath the first cut, and, with a pair of scissors, the skin is cut out together with the orbicularis (1.0 to 1.5 mm). In those serious cases where the tarsus is greatly thickened, it is cut away up to half of its size. To close the wound, four to five simple stitches are made; these are removed after nine or 10 days.

Since I modified the Kuhnt operation by introducing the cuneiform cuts, I have done several thousand of these operations, always with excellent results.

P.O. Box 234.

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THE EFFECT OF CHLORPROMAZINE (THORAZINE) ON INTRAOCULAR PRESSURE IN EXPERIMENTAL ANIMALS*

SATYA DEV PAUL, D.O., AND IRVING H. LEOPOLD, M.D.
Philadelphia, Pennsylvania

The present study was done to evaluate the influence of chlorpromazine (Thorazine) on intraocular pressure.

Since the paper of Bierent[1] advocated the use of chlorpromazine in cases of glaucoma, especially acute glaucoma in which he found it to be an excellent regulator of the neuro-autonomic system in its ocular circuit, it was felt by us that the uses of chlorpromazine in clinical ophthalmology needed further investigation.

EXPERIMENTAL METHODS

For investigational purposes rabbits (pigmented and albino) and cats were selected. Chlorpromazine was administered to these animals by two routes: (1) Intramuscular injections and (2) topical application to the eye.

The determination of a suitable dose for intramuscular injection presented a difficult problem, as in the literature various dosages have been employed to study the various effects of the drug. It was decided to start from the standard dose of 25 mg./cc. (as marketed by Smith, Kline & French). The maximum dosage given was of 100 mg. in a single injection.

In topical use, 2.5-percent and 1.0-percent chlorpromazine (Thorazine) solutions were employed.

INTRAMUSCULAR THORAZINE

TECHNIQUE

Rabbits. All rabbits were weighed and tagged for comparison purposes. The eyes were anesthetized by topical application of pontocaine (0.5-percent solution). The size of the pupil was noted and the tension of both eyes was taken with a Schiøtz tonometer, and tonometry was repeated after an average interval of 35 minutes. Then an intramuscular injection of Thorazine was given and tonometry was done after every hour.

Cats. The cats were anesthetized with intraperitoneal pentobarbital sodium (Nembutal) prior to any tonometry. After anesthetization, the size of the pupil was noted and the tension with a Schiøtz tonometer was taken on both eyes and the procedure repeated after 45 minutes to get an average.

Intramuscular Thorazine injection was given and the tension was measured every hour.

The behavior of the intraocular pressure in these two different groups of animals with different doses can be summarized as follows:

RABBITS

A

Six pigmented rabbits were employed to study the effects of a 25-mg. intramuscular injection of Thorazine.

Within the first hour of injection of Thorazine, the following changes were noted:

1. All eyes showed a drop in intraocular pressure ranging from 1.0 to 6.0 mm. Hg.
2. In five animals there was a relative miosis.

All these animals were under observation for a period of five hours after injection of Thorazine. To summarize the results of 25 mg. intramuscular injections of Thorazine (fig. 1):

1. The maximum effect of the drug was obtained between two to four hours after the injection.
2. All six animals showed a lowering of

* From the Research Department, Wills Eye Hospital. Chlorpromazine (Thorazine) was supplied by the courtesy of Smith, Kline & French, Philadelphia.

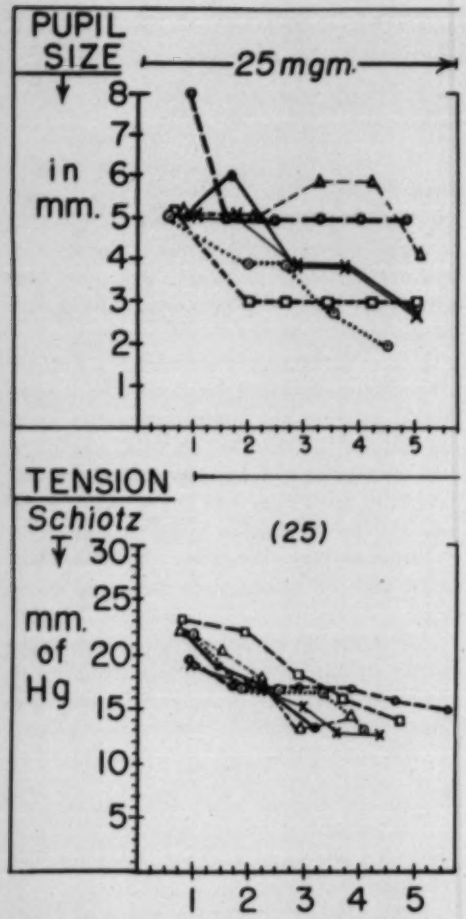

Fig. 1 (Paul and Leopold). Effect of Thorazine on the intraocular pressure and the size of pupil in rabbits (25 mg. of Thorazine administered intramuscularly). Intraocular pressure measured with a Schiøtz tonometer (5.5 gm.); pupil size measured with calipers and a mm. rule. Time in hours.

intraocular pressure of between 5.0 to 8.0 mm. Hg.

3. The pupil was miotic in all six rabbits.

B

Six albino rabbits weighing between five and six and one-half lb. were given 50 mg. of Thorazine. Within one hour of injection of the drug the lowering of intraocular pressure was 2.0 to 9.0 mm. Hg. Three rabbits had mydriasis. All these animals were observed for a period of five hours after injection (fig. 2):

1. The maximum effect of the drug was obtained within two to four hours of injection.

2. The lowering of intraocular pressure ranged from 5.0 to 12 mm. Hg.

3. All animals were miotic.

C

An intramuscular injection of 75 mg. of Thorazine was administered to six rabbits with weights ranging from four and one-half to six lb.

Within one hour of the injection, the lowering of tension was 2.0 to 8.0 mm. Hg. Three animals showed miosis. These animals

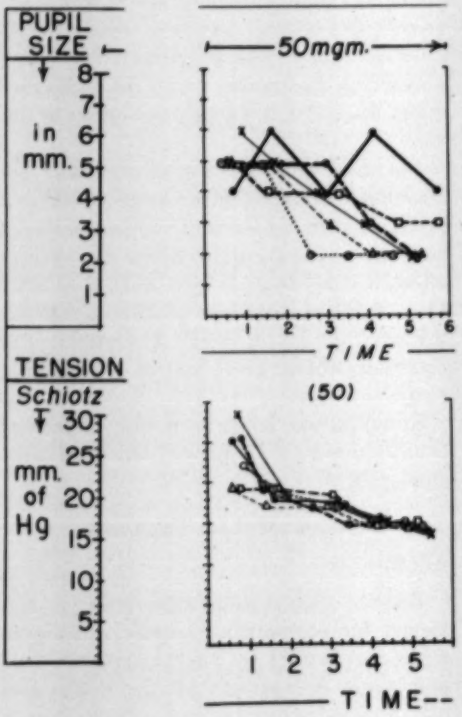

Fig. 2 (Paul and Leopold). Effect of Thorazine on the intraocular pressure and the size of pupil in rabbits (50 mg. of Thorazine administered intramuscularly).

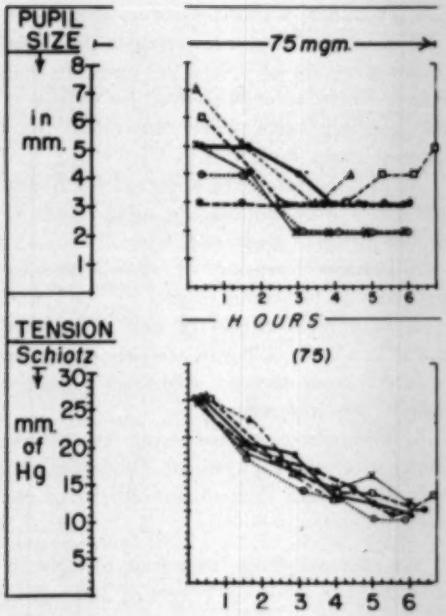

Fig. 3 (Paul and Leopold). Effect of Thorazine on the intraocular pressure and the size of pupil in rabbits (75 mg. of Thorazine administered intramuscularly).

were observed up to six hours after the administration of Thorazine (fig. 3):

1. The maximum lowering of tension was obtained within two to five hours after injection of Thorazine.
2. The lowering of tension ranged from 12 to 14 mm. Hg.
3. All six rabbits showed miosis.
4. One rabbit died during the experiment.

D

For the experiment with the intramuscular administration of 100 mg. of Thorazine, five rabbits of weights ranging from five to six lb. were used. Within one hour of injection of Thorazine, the lowering of tension ranged from 12 to 16 mm. Hg. and, in four animals, was accompanied with miosis.

All these animals were observed for a period of six hours after the administration of Thorazine. The conclusions derived from these observations were (fig. 4):

1. Definite lowering of tension (12 to 20 mm. Hg) occurred in all animals.
2. Two and one-half to three and one-half hours after the injection, the effects of the drug were most marked.
3. All animals showed miosis in the end.
4. The dose was fatal to two animals which exhibited marked lowering of intraocular pressure 20 to 30 minutes prior to death and had convulsions before they died.
5. Five hours after the injection of Thorazine, the tension showed a rise toward the original tension recorded.

Cats

A

Six cats weighing from four to eight lb. were used to study the effects of intramuscular injection of 50 mg. of Thorazine. The same procedure as already described was carried out.

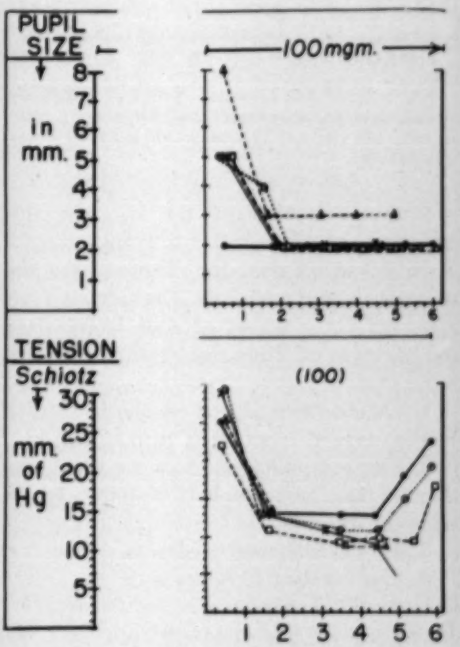

Fig. 4 (Paul and Leopold). Effect of Thorazine on the intraocular pressure and the size of pupil in rabbits (100 mg. of Thorazine administered intramuscularly).

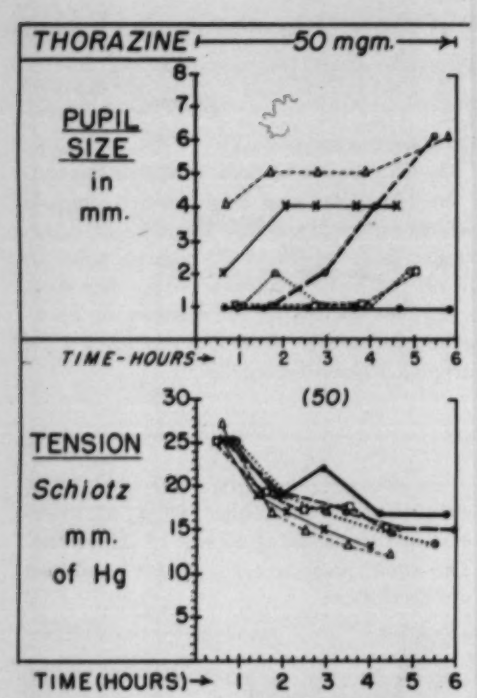

Fig. 5 (Paul and Leopold). Effect of Thorazine on the intraocular pressure and the size of pupil in cats (50 mg. of Thorazine administered intramuscularly).

Within one hour of the injection, the lowering of intraocular pressure ranged from 7.0 to 9.0 mm. Hg. Three of the six animals showed mydriasis. The animals were observed for a period of four hours after the injection of Thorazine. The conclusions were (fig. 5):

1. Definite lowering of tension in all cats studied ranged from 10 to 16 mm. Hg.
2. The maximum effect of the drug was reached two and one-half to three hours after the injection.
3. Five cats showed mydriasis.
4. One cat died 12 hours later.

B

Six cats weighing from four to eight lb. were employed to study the effect of 75 mg. of Thorazine by intramuscular injection. The procedure was the same as described.

Within one hour, a lowering in the intraocular pressure of 4.0 to 9.0 mm. Hg was noted. Three animals showed no change in the pupillary size while the other three showed slight mydriasis.

All the animals were observed for five to six hours after the injection. The results of this experiment were (fig. 6):

1. Definite lowering of the intraocular pressure 14 to 16 mm. Hg.
2. Maximum effects of the drug were noted two to three hours after the injection.
3. All cases showed mydriasis when the tension was lowered.
4. The tension started rising four to five hours after the injection of Thorazine.
5. No animal died of the effects of the drug.

Six cats weighing from four to eight lb. were used to study the effects of 100 mg. of Thorazine by the intramuscular route. The experiment was carried out by the same technique.

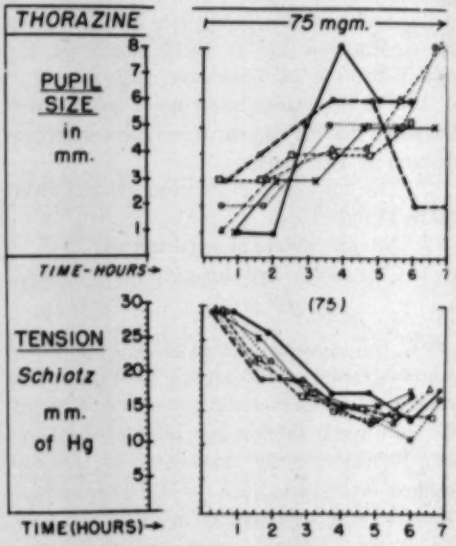

Fig. 6 (Paul and Leopold). Effect of Thorazine on the intraocular pressure and the size of pupil in cats (75 mg. of Thorazine administered intramuscularly).

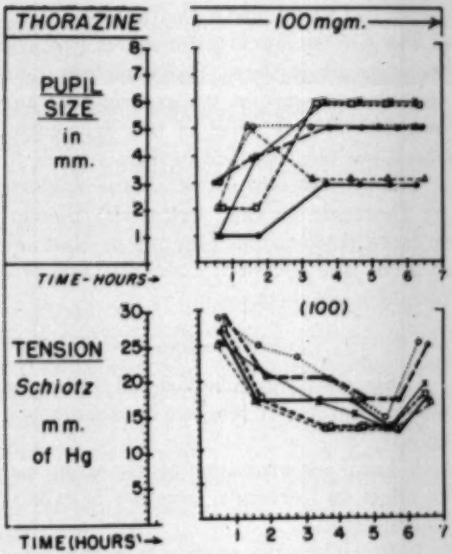

Fig. 7 (Paul and Leopold). Effect of Thorazine on the intraocular pressure and the size of pupil in cats (100 mg. of Thorazine administered intramuscularly).

Within one hour after injection, the lowering of the intraocular pressure was from 2.0 to 8.0 mm. Hg. Four cats out of six showed mydriasis. All the animals were observed for five to six hours after the injection. The results of the experiment were (fig. 7):

1. Lowering of the intraocular pressure 12 to 16 mm. Hg.
2. Maximum effects of the drug were noted within three to four hours of administration.
3. Marked mydriasis in all cases.
4. No fatality.
5. A tendency of the tension to rise within the fifth hour after administration of the drug.

Effects of topical application of Thorazine

The animals employed were mainly rabbits ranging from 4.25 to 5.25 lb. in weight. Chlorpromazine (Thorazine) was used in 2.5-percent to 1.0-percent solutions.

The rabbits were wrapped in eye sheets and pontocaine (0.5 percent) was used as a local anesthetic. Tension was taken with Schiøtz tonometer prior to the administration of Thorazine. The drug was instilled locally in the eye (lower conjunctival cul-de-sac) every 15 to 20 minutes. Tonometry was done after 45 minutes.

A

Six rabbits were used to observe the effect of 2.5-percent Thorazine solution. No appreciable lowering of tension was noted. All rabbits showed a relative miosis.

Toxic signs noted were: (1) Marked chemosis and injection of the conjunctiva; (2) conjunctival discharge markedly increased; (3) the corneas were extremely hazy; (4) the corneas stained uniformly with fluorescein; (5) de-epithelization of the cornea.

Twenty-four hours later all animals had marked ciliary and conjunctival injection. The cornea was still hazy and there were signs of uveitis.

It appeared from the above experiment that Thorazine in a 2.5-percent strength was very irritative and toxic to the eye.

B

Four rabbits were used to study the effect of one-percent Thorazine solution. No appreciable lowering of intraocular pressure was noticed. The size of the pupil remained about the same. The conjunctival discharge was about two plus. The conjunctiva was injected. The cornea was clear.

It appears that one-percent Thorazine solution is less irritating than 2.5-percent solution but neither strength lowered the intraocular pressure.

Summary

In this series of experiments Thorazine was tried on 34 rabbits and 18 cats. The most effective lowering of the intraocular pressure was obtained by the intramuscular route. Topical application showed no hypotensive action and was irritating.

The use of 25 mg. of Thorazine had a slight effect on the intraocular pressure and had no lethal action on the rabbits.

Maximum lowering of the tension was obtained by the administration of 75 mg. of Thorazine. This dose was not fatal to cats. The behavior of the pupil differed in these two groups of animals; in cats it was invariably mydriatic, while in rabbits it was miotic. The maximum effect of the drug is at least two hours after the injection. The lowered tension did not persist, for, on longer observation, it showed a tendency to rise.

The administration of 100 mg. of Thorazine had fatal results in half of the rabbits. The cats were, however, resistant to the toxic effects of the drug. The results of the experiment with 100 mg. were similar to those obtained after administration of 75 mg.

It was observed that Thorazine had a relatively better hypotensive effect on those eyes which had an original higher tension.

The present work demonstrates that systemically administered Thorazine lowers intraocular pressure in the experimental animal. The site of effect of this hypotensive agent was not identified in these studies.

Clinical lowering of intraocular pressure by Thorazine has been reported by Bierent[1] in acute glaucomatous eyes and by Nutt and Wilson[2] who employed Thorazine as a preoperative anesthetic agent.

Conclusions

1. Systematically administered Thorazine lowered intraocular pressure in experimental animals.

2. Local administration of Thorazine had no effect on intraocular pressure in experimental animals.

3. In rabbits the pupil was miotic after systemic administration of Thorazine, while in cats it was mydriatic.

1601 Spring Garden Street (30).

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PRECANCEROUS CONDITIONS OF THE BULBAR CONJUNCTIVA*

Gyula Lugossy, M.D.
Budapest, Hungary

By precancerous conditions are meant those changes which, although not yet malignant, are prerequisite to cancer formation; cancer is developed as a secondary disease (Hamperl,[6] Dietrich[4]).

Such conditions of the bulbar conjunctiva and the corneal limbus were recognized and described over a hundred years ago by Bowman.[3] Since then, many authors have reported similar cases: Warlomont,[21] Hocquart,[9] Gallenga,[5] Best,[2] Mohr and Schein,[15] Saemisch,[18] Jervey,[11] McGavic,[14] Ash and Wilder,[1] Hertzburg,[8] and so forth. The changes were variously termed: tyloma (Vassaux,[20] Wedl and Bock,[22] Gallenga,[5] Stock[19]), hornification of the conjunctiva (Best[2]), keratosis (Mohr and Schein[15]), conjunctival callosity (Saemisch[18]). The essence of the rather infrequent morbid condition is the local hyperplasia and hornification of the conjunctival and corneal epithelium. This is best reflected by the term "epithelial plaque," which was first applied to precancerous conditions of the bulbar conjunctiva by Lister and Hancock[13] in 1903.

* From the Department of Ophthalmology, State Institute of Rheumatism and Balneology.

Today, this is the name most often used in literature.

Nicholls[16] divided the varieties of the conjunctival and corneal epithelial plaques into three groups:

1. The epithelial plaques found with xerosis.
2. Congenital plaques.
3. Those secondary to chronic irritations of the conjunctival sac. In the group, two subgroups have been distinguished: (a) Moderate hornification and hyperplasia of the epithelium, and (b) hornification and considerable, rapidly growing hyperplasia which is similar to, or identical with, leukoplakia found in other parts of the body (acanthosis, hyperkeratosis, dyskeratosis of the epidermis, and varying chronic inflammatory reactions in the subepithelial tissue).

Epithelial plaques may occur on the corneal epithelium (Wilson[24]) or on any area of the bulbar conjunctiva. Such plaques appearing at the corneal limbus were reported by Heilbrun,[7] McGavic,[14] Ash and Wilder,[1] Kennedy and Sullivan,[12] and others. The plaque described by Wollenberg[25] was covered by the lower lid, the one reported by Mohr and Schein[15] by the upper lid. The plaque is, however, most frequently found within the palpebral fissure, as in my cases.

Case reports

Case 1

N. J., a 20-year-old man, wished to be operated for a small nodule which had been growing on his left eye for a month and caused foreign-body sensation. The patient was well developed and nourished. His vision was normal in both eyes. Examination revealed a colored, pinhead-sized, grayish-pink plaque on the left bulbar conjunctiva, about 0.5 cm. from the temporal border of the cornea. It was rather well limited, devoid of any inflammatory reaction, and movable. Otherwise, the globes were normal.

After anesthesia with cocaine solution the plaque was excised in such a way that cutting took place in intact tissue. The neighboring conjunctiva was dissected off, then the wound was closed by three interrupted sutures. Recovery was uneventful; a lineal scar remained. No recurrence has been observed during five years.

The removed growth was fixed in formalin and embedded in paraffin. Its histologic examination (A. Kálló, chief pathologist) revealed:

The covering stratified epithelium is markedly broadened, its projections are deep, elongated, distorted (acanthosis). Though this anomaly of the epithelium displays no malignancy, its irregularity represents a precancerous condition.

Discussion. At that time, I did not intend to publish this case, therefore neither a photo nor photomicrographs were made of the plaque. An epithelial plaque resembling that of my patient may be seen in the paper of Kennedy and Sullivan[12] (Case 2, fig. 1). The plaque of Figure 1[12] differs from that of my patient in its vascularization. These circumscribed subconjunctival-episcleral vascularizations are, as stated by Papolczy,[17] constant accompanying phenomena of epibulbar cancers. Although no mention is made of a cancer in the histologic findings of Kennedy and Sullivan's case and the published photograph does not show cancerous changes, the thought may arise that an intraepithelial (pre-invasive, in situ) carcinoma might have been present.

This thought is still more valid for Cases 1 and 3 of Kennedy and Sullivan.[12] In both of these cases, the epithelial plaque situated at the limbus had already extended to the cornea. Further, tortuous vessels run to the plaque.

The clinical course of this case exhibits much similarity to another of my cases.

Case 2

K. I., a 45-year-old woman, asked for removal of the "proud flesh" which had been growing on her right eye for a year. There was, on the inner border of the right cornea at the 3-o'clock position, a lentil-shaped,

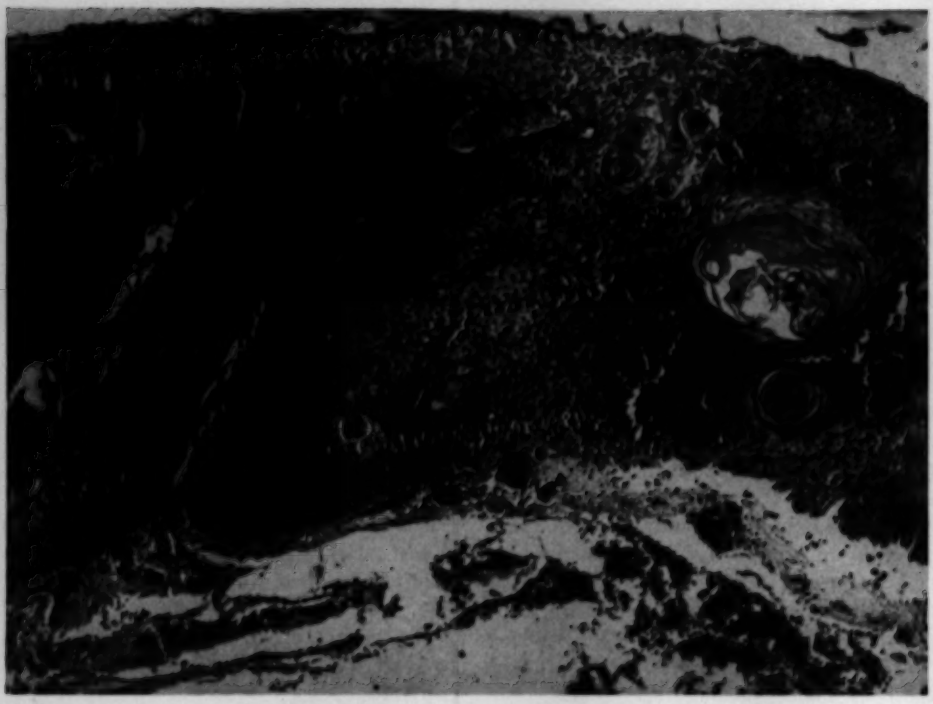

Fig. 1 (Lugossy). Squamous-cell carcinoma.

grayish-pink structure of the papillary surface, measuring 4.5 mm. in length, 5.5 mm. in width, and 2.0 mm. in height. One third of the growth was situated on the cornea, two-thirds were on the sclera. Its lower borderline was mildly pigmented. There were two thick, tortuous vessels running from the inner angle of the eye toward the structure, one above and one below. The growth adhered firmly to its base. Its most prominent and lightest part was above the cornea.

The lesion was removed with a lancet. Cauterization of its site was followed by conjunctival keratoplasty. Later, histology disclosed the tumor to be a squamous-cell carcinoma (fig. 1). The scanty pigment found in the tumor cells was hematogenous, since the corium beneath the tumor contained large blood sinuses and extensive hemorrhages surrounding this area (Kálló).

Evidently, the epithelial plaques and similar changes of the bulbar conjunctiva should be given minute attention. The clinical picture is not always sufficient for an accurate diagnosis. Initially, the lesion may simulate a pinguecula or especially a pterygium. In cases of pronounced vascularization, an epibulbar cancer rather than precancer is, as pointed out by Papolczy,[17] to be taken into consideration. In four of his patients the correlation of pterygium and cancer was verified histologically. In two other patients, the correlation was probable.

Regarding the uncertainty of the clinical picture, Wilson[23] suggested examining these changes under ultraviolet light—pingueculas and pterygia fluoresce, epithelial plaques do not. Reliable diagnosis depends on histologic diagnosis.

The opinion that these epithelial plaques do, like leukoplakia, represent precancerous conditions has been fortified by the recur-

rences which have been observed. In Wollenberg's patient,[25] roentgen therapy and, in the patient of Jacqueau and Bujadoux,[10] curetting and cauterization were followed by recurrence. Therefore, early surgical removal is the best method. This can be combined with postoperative irradiation if histologic examination reveals its necessity.

Summary

Precancerous conditions occurring on the bulbar conjunctiva are discussed. Epithelial plaques are rare. They are identical with leukoplakias occurring at other sites (acanthosis, hyperkeratosis, dyskeratosis of the epidermis, and chronic inflammatory reactions of varying degree in the subepithelial tissue). If the plaque is surrounded by subconjunctival-episcleral vascularization, carcinomatous degeneration is to be taken into consideration. Recurrences or cancer formation can best be prevented by the early excision of the epithelial plaque.

State Institute of Rheumatism.

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PARENCHYMATOUS ORIGIN OF FILAMENTARY KERATITIS

New histopathologic concepts

Carlos Weskamp, M.D.
Rosario, Argentina

Filamentary keratitis is essentially a chronic disease of the cornea of unknown origin. The condition is characterized by the sudden appearance of small semitransparent prominences upon the apparently normal epithelium of the cornea. The protuberances are smaller than a pinhead but grow rapidly and may reach a length of six to eight mm. having the appearance of threads or filaments. With the movements of the eyelids and of the globe, the filaments coil upon themselves in corkscrew fashion and finally, due to strong pull, they fall off. But they recur shortly and the patients—generally

middle-aged women—complain of foreign-body sensations.

The condition is usually unilateral. There can be two or more threadlike formations in one eye.

Filamentary keratitis thus defined excludes the threadlike formations composed of capsular debris, vitreous humor, and so forth, subsequent to trauma either surgical or of any other kind. The present definition excludes as well the filamentary exudative masses produced by the inflamed conjunctiva and adherent secondarily to the corneal surface.

In the year 1882, at Heidelberg, Leber[1] reported for the first time upon three cases of this rare disease which "seemed related to herpes corneae." He stated also: "These fine threads have a peculiar structure; they consist of a cord axially coiled, fibrillar in nature, lined by a looser cortical sheath, which like the cord itself also contains cellular elements and several micrococci. The surface is partly covered by epithelial cells." Leber believed that these formations were coagulation products originating from the conjunctiva.

About the same time, Uhthoff described another case but I could not find his report in the literature available here. Uthoff himself mentioned this report in 1889, at the 20th meeting of the Ophthalmological Society of Heidelberg, when discussing a paper presented by Fischer. Uhthoff's[2] words were: "I believe that those fine threads are a true exudative formation from the superficial layers of the cornea. The exudates find their way toward the surface and, assuming the shape of fine threads, they remain attached to the cornea for some time. I take the opportunity to correct my former opinion stated in my publication and according to which I considered that those filaments could possibly be pieces of Bowman's membrane. I thought it was Bowman's membrane that would spring out and twist or coil itself like a cord." Leber,[3] attending the same meeting, ratified his belief that the filaments were of conjunctival origin and incidentally adherent to the cornea.

Fischer,[4] whose report brought forth the discussion just mentioned, stated that the filaments were due to secretions of the inflamed cornea. He compared this finding with the filaments which Curshman and Pel, Amsterdam, found on the bronchial surface in certain cases of asthma.

Two years later Czermak[5] stated that the filaments adherent to the cornea were due to exudates produced by the conjunctiva, and he believed that "filamentary keratitis" should not be considered a nosologic entity. He referred to filaments attached to the cornea in patients with traumatic keratitis; in three cases the filaments appeared after surgical trauma of the eye, and in one case after lime burns. After studying these four cases, I draw the conclusion that they cannot be related to filamentary keratitis, at least not according to my definition of the disease. Czermak's cases should be grouped under the heading of pseudofilamentary keratitis.

As to the origin of the fine threads in filamentary keratitis, no agreement existed until Hess[6] and especially Nuel[7] undertook the histopathologic study of the filament. These authors settled positively that the filaments did not originate from the conjunctiva, secondarily adhering to the cornea, but that they originated from the cornea itself.

Nuel not only studied the filament—as other authors did—but also examined a small superficial portion of corneal tissue, where either a filament or any small elevation that precedes the formation of the thread was attached. His aim was to study the site of attachment of the filaments. Then he reported:

"Filamentary keratitis is a disease of the corneal epithelium and secondarily of the bulbar conjunctiva. Its nature is rather hypertrophic. . . ."

Vogt[8] describes the disease, in his *Atlas*, under two headings, one in German and one in Latin, the literal translation of the former

being "thread-keratitis" and of the latter "epithelial filamentary keratitis."

Duke-Elder[9] describes the disease in his *Textbook of Ophthalmology* under the heading of changes in the epithelium.

Until now it is agreed that the filament attached to the cornea arises from the corneal epithelium.

According to my views the aforementioned statements are not exact as long as they are based only on examinations of the filament and of its point of insertion at the epithelium. My histologic investigations of the epithelium and of the stroma show that the filaments do not arise from the corneal epithelium but from the stroma itself. The whole process can be compared to the birth of a volcano.

The material for my study was obtained from two women patients, aged 46 and 48 years, respectively, both suffering from typical filamentary keratitis. A specimen for biopsy was obtained from each case; the specimens were almost square in shape, 4.0 by 4.0 or 5.0 by 5.0 mm., the total amount of the surface being from 15 to 20 sq. mm. They consisted of epithelium and stroma to almost half the total thickness of the cornea. The postoperative course was uneventful and without further impairment of vision. The material was fixed in Bouin's solution, embedded in paraffin, and stained according to routine methods.

The filaments were studied separately and their histologic appearance revealed nothing that might be added to the descriptions already known.

It was the seriated corneal sections that revealed most interesting findings. In Figure 1 may be seen a portion of cornea next to the site of attachment of a filament. A striking fact can be observed: namely the integrity of the epithelium and of Bowman's membrane, in spite of the fact that the superficial parenchyma is altered. The lamellae which normally constitute the parenchyma have turned into fibrils. That would represent the first phase of the morphologic alteration of the process.

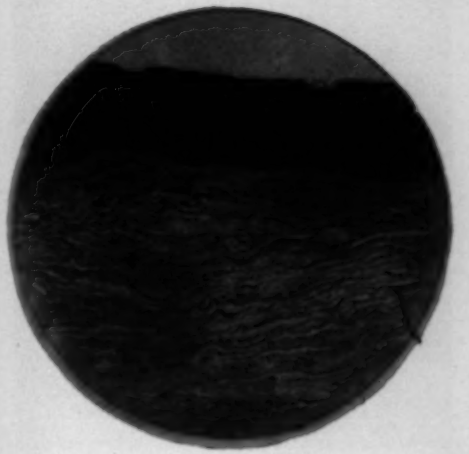

Fig. 1 (Weskamp.) (Drawing. Inclusion 789-Slide 40). Portion of cornea next to a filament. The epithelium and Bowman's membrane are intact. The lamellae of the superficial parenchyma have turned into fibrils.

These changes are more clearly seen in Figure 2, where one can also observe an alteration in Bowman's membrane, as demonstrated by the areas more intensely stained.

Figure 3, a section of the same specimen as described in Figures 1 and 2, exhibits two very interesting aspects of the changes in the subepithelial parenchyma, namely the presence of small dilated capillary vessels and macrophages. But the most striking feature is that the subepithelial stroma has turned into a homogeneous substance of gelatinoid appearance, that filters between the epithelial cells and surrounds a group of these cells. The epithelial cells lying directly upon the gelatinoid substance have suffered a metabolic disturbance and their orderly arrangement is altered. The intercellular spaces are clearly seen, due to interstitial edema. At places Bowman's membrane assumes a serrate appearance, like a saw, beneath the epithelium; at other sites Bowman's membrane shows darker stain at intervals, appearing like dashes.

Figure 4 shows very clearly the amorphous substance penetrating the epithelium

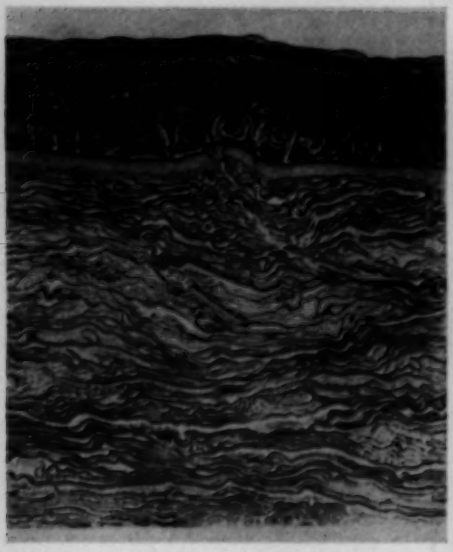

Fig. 2 (Weskamp.) (Drawing. Inclusion 789-Slide 39). The altered parenchyma at Figure 1 appears more clearly. Bowman's membrane stains more intensely at its border with the epithelial cells.

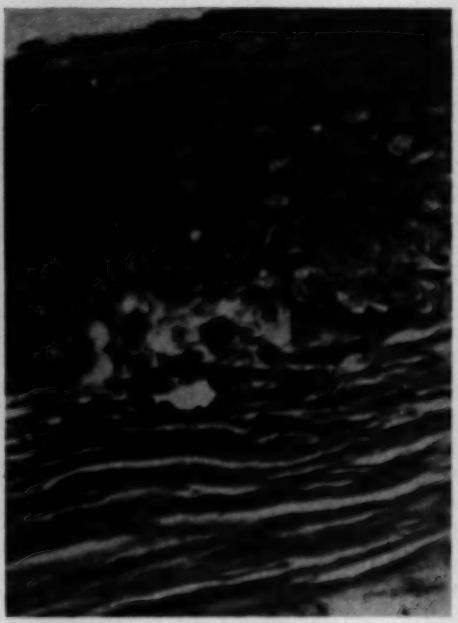

Fig. 3 (Weskamp.) (Inclusion 789-Slide 1). The subepithelial parenchymatous tissue has become a homogeneous gelatinoid substance that creeps between the epithelial cells. There are small dilated capillaries and macrophages. Interstitial edema is present.

Fig. 4 (Weskamp.) (Inclusion 789-Slide 2). The subepithelial amorphous substance has penetrated the epithelium and surrounds a group of cells, encircling them as within a pen. Many of these cells appear degenerated.

Fig. 5 (Weskamp.) (Inclusion 789-Slide 5). The parenchyma has penetrated the epithelium. The epithelial cells are altered and destroyed as if to clear the way for the advancing parenchymatous product that tends to emerge toward the surface.

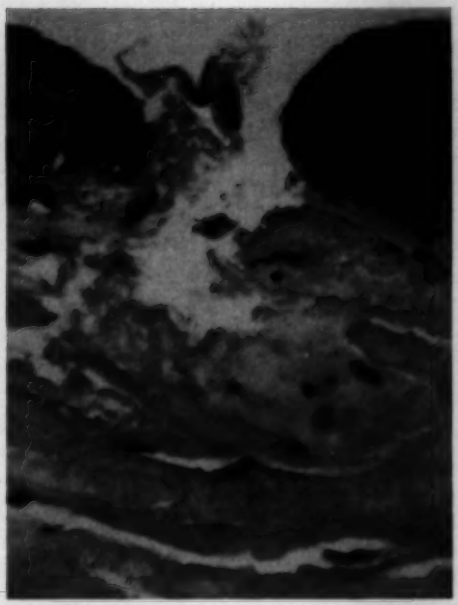

Fig. 6 (Weskamp.) (Inclusion 817-Slide 14). Section showing the place through which a filament has pierced its way toward the surface and finally fallen off. The epithelium next to the ruptured place is normal, but the parenchyma shows a defect also, as well as changes similar to those described in previous pictures.

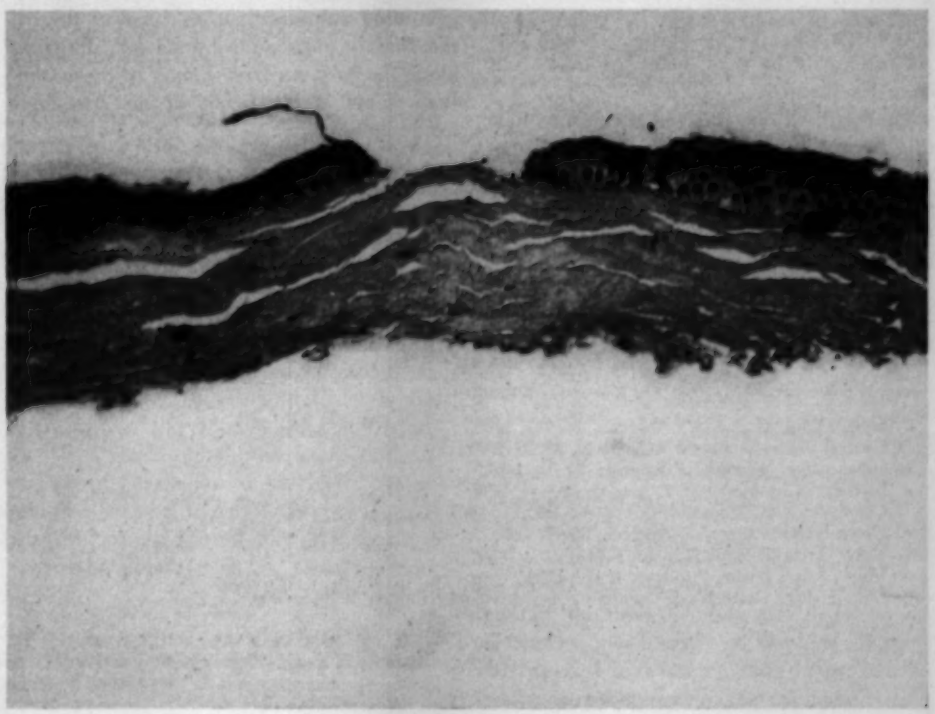

Fig. 7 (Weskamp.) (Inclusion 817-Slide 7). One can see the site of attachment of a filament and a strip of epithelium that has not yet detached itself.

Fig. 8 (Weskamp). (Inclusion 817-Slide 8). Section showing parenchymatous disturbances, as described in preceding pictures, and the repair of the epithelial hole by new cells.

and encircling a group of cells as in a pen. As can easily be seen, many of these cells have degenerated.

In Figure 5 one can see once more how this amorphous substance pierces the epithelium. The epithelial cells are altered and destroyed, as if making room for the parenchymatous product working its way toward the surface.

Figure 6 exhibits the site through which the filament has come out and fallen off. The epithelium surrounding the ruptured place is absolutely normal. It is hard to believe that there was ever any epithelial change so close to this normal zone. At the stroma, however, there is an empty space, owing to a defect, and other parenchymatous changes, as already described, are present.

Figure 7 demonstrates the place where a filament was attached; one can also see an epithelial tag that has, as yet, failed to fall off.

Summary

The first change observed in filamentary keratitis takes place in the parenchymatous lamellae underlying Bowman's membrane. Initially the lamellae turn into fibrillar bundles and finally become a homogeneous substance of gelatinoid appearance. This substance invades the epithelium, traverses Bowman's membrane, and encircles groups of epithelial cells. These cells, enclosed and disintegrated by the invading substance, lose their vitality. Under these circumstances, the gelatinoid substance makes its way toward the surface and finally bursts out, dragging along the most superficial layer of the epithelium. This is the result of my histologic examination.

Comment

In the present paper I have tried only to demonstrate that the filaments do not originate from the epithelium but from the substantia propria.

Laprida 1159.

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NOTES, CASES, INSTRUMENTS

OPHTHALMIC USE OF TYZINE*

A CLINICAL STUDY OF THIS NEW VASOCONSTRICTOR

ERWIN E. GROSSMANN, M.D., AND ROGER H. LEHMAN, M.D.
Milwaukee, Wisconsin

Ophthalmologists see many cases of hyperemia of the palpebral and bulbar conjunctivas. Whether this hyperemia is primary, as in the so-called chronic conjunctivitis, or secondary to injury, infection, allergy, or disease of other portions of the eye, symptomatic relief can be afforded by the use of topical agents which bring about decongestion by vasoconstriction. Photophobia, often a concomitant complaint of hyperemia, is also frequently relieved by decongestion.

Insults to the eye from whatever noxious agency can set up a vicious cycle—the discomfort of hyperemia leads to further irritation by rubbing the eyes, which then produces further hyperemia. If this cycle is not interrupted by the successful use of a decongesting agent, weeks or months of distress can result.

The features which make a desirable ophthalmic decongestant are several: (1) The solution should be stable as regards potency and pH at the extremes of room temperature. (2) The onset of decongestant action should be rapid, and the effect prolonged. (3) There should be an absence of rebound vasodilatation. (4) It should be nonirritating. (5) There should be no significant sympathetic systemic effects. (6) There should be little or no accompanying mydriasis or cycloplegia, for not only do these cause disagreeable photophobia and visual difficulty but also increase the risk of precipitating symptoms in an eye predisposed to glaucoma.

There are several agents in common use which have been carefully evaluated. Paredrine hydrobromide was found useful in cases of chronic conjunctivitis in older people because of the absence of mydriasis and cycloplegia.[1] Its effects, however, were not vigorous and lasted generally about an hour. Phenylephrine hydrochloride (Neosynephrine) was found to be a useful and reliable agent, but consistently produced mydriasis.[2] Naphazoline (Privine) used as a nasal decongestant has resulted in rebound vasodilatation of such marked degree that it could be controlled only by a prolonged and uncomfortable period of refraining from all medications.[3-5] Since no such ill effects were encountered in one study of the ophthalmic use of naphazoline, it was thought to be a satisfactory decongesting agent and superior to phenylephrine.[6]

This paper deals with the ophthalmic use of a new sympathomimetic agent, Tyzine, which is designated chemically as 2-(1,2,3,4 tetrahydro 1-naphthyl) imidazoline hydrochloride. It is similar to other sympathomimetic agents in that it contains an aromatic nucleus and an amine group but differs basically in that the aromatic ring and the amine group are separated by one, rather than two, carbon atoms, and the aromatic nucleus consists of one saturated and one unsaturated ring. Previous observations have indicated that Tyzine is free of systemic pressor action and does not stimulate the central nervous system when used topically.[7]

Several recent papers have dealt with the use of Tyzine as a nasal decongestant,[8,9] and the results indicate that, in respect to speed of onset, duration of effect, lack of rebound phenomena, and absence of systemic effects, it is superior to other available decongesting agents. No references to the ophthalmic use of Tyzine were found.

* From the Department of Ophthalmology, Marquette University School of Medicine. The preparations of Tyzine used in this study were furnished through the courtesy of Dr. M. Carlozzi of Chas. Pfizer & Co., Inc.

Materials and Methods

Ninety-four patients were treated with Tyzine for conjunctival hyperemia due to a variety of ophthalmologic conditions including chronic hyperemia, chemical and physical trauma, blepharitis, actinic conjunctivitis, thyrotropic exophthalmos, recurrent chalazia, and keratitis.

The degrees of hyperemia of the cases chosen ranged from mild injection to severe congestion and inflammation.

The solution used was Tyzine in an 0.1-percent concentration with a pH between 5.5 and 6.5. Dosage was two drops of this solution three times a day for two to 30 days. Tests were carried out in one eye only, and the length of time necessary to blanch the conjunctiva was noted. Evaluations were recorded for the onset and duration of action, the presence or absence of rebound hyperemia, the occurrence of mydriasis, the presence or absence of a true anesthetic effect, the stability of the solution at the extremes of room temperature, and, most importantly, the therapeutic result as indicated by relief of symptoms.

Following the initial group of patients, an additional 62 cases were treated in an effort to evaluate the effectiveness of an 0.05-percent solution as compared with the 0.1-percent solution.

Results

Good to excellent therapeutic effects were noted in all patients. In 65 of the patients, detailed observations were made concerning rapidity of response and duration of action; these results are seen in Table 1.

The sensation of relief was so marked in many of the patients that an anesthetic effect was suspected. Therefore, corneal sensitivity was tested on minute after the instillation of Tyzine in one eye and of normal saline in the other. It was found that corneal reflexes were unaltered, there being no difference between the saline-treated and the Tyzine-treated eyes.

In order to determine the stability of the solution at room temperature extremes, portions were placed for 24 hours in the refrigerator and in the incubator. There was no indication that stability was altered.

Tyzine was used on many patients who had had a nonspecific hyperemia of the conjunctiva—ones who had tried many therapies without satisfactory results. These patients had used antibiotic drops, Privine, preparations containing zinc, and the proprietary solution, "Murine." In all cases the comfort the patient received indicated Tyzine was superior. It was also noted that after the effects of vasoconstriction had subsided the eyes did not become more red than previously, indicating an absence of rebound vasodilatation.

In the tests carried out comparing the result of treatment with the 0.05-percent solution and 0.1-percent solution in an additional 62 patients, the weaker solution was found to afford the same degree of relief, to produce more immediate blanching, and to have a duration of action approximately the same as the stronger solution.

TABLE 1

Therapeutic responses in 65 patients

A. Time for eye to become white (in seconds)	<20	20–30	30–45	>45
Number of patients	36	19	6	4

B. Duration of effect (in hours)	<1	2–3	3–4
Number of patients	4	6	55

Conclusions

The results of this study indicate that Tyzine will become useful in the treatment of many patients who complain of burning, irritation, scratchy sensations, and so forth. In these patients, mild conjunctival hyperemia is frequently the only finding. The hyperemia is aggravated by wind, dust, smoke, and, often, alcohol. There appears to be no infective element. In this type of patient, Tyzine appears to give immediate relief. It was our impression that the results were better than those obtained with Privine, and with 0.125-percent Neosynephrine. The Tyzine not only was more comfortable to use but the decongestive effect seemed far superior. The only solution that matched Tyzine in vasoconstricting activity was a 1:1,000 solution of adrenalin. Adrenalin of course is unstable, does not have a soothing sensation, has undesirable systemic side effects, and is a potent mydriatic as well.

In the cases of specific disease in which Tyzine was used, it appeared to be of great benefit whenever there was edema, swelling, or congestion. Many cases of itching were relieved almost immediately on instillation. There was no effect on pupil size in any patient. No toxic manifestations were observed.

It would appear that the 0.05-percent and the 0.1-percent solutions are equally effective.

Summary

A new vasoconstrictor, Tyzine, was used on a total of 156 patients. The results seemed to indicate that Tyzine is an excellent ophthalmic decongestant, superior to all other commonly used drugs of similar nature and purpose.

238 West Wisconsin Avenue (3).

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EQUIPMENT*

For objective determination of visual acuity according to Goldmann

Theo Schmidt, M.D.†
Bern, Switzerland

Principle of the instrument

Visual acuity is characterized by the minimum angular distance at which two points are just visible separately (minimum separable). If this perception can be deduced from an involuntary physical reaction of the patient, then we speak of an objective determination of visual acuity. The physical reactions in question are eye movements, optokinetic nystagmus, or optokinetic pendular movements. These last mentioned movements

* Manufactured by Haag-Streit, Liebefeld-Bern, Switzerland.

† From the Eye Clinic of the University of Bern. Director: Prof. H. Goldmann.

are employed in Goldmann's method of objective determination of visual acuity.

The stimulus which induces the involuntary eye movements, in the person examined, is a board with a checkered stripe on a uniform background which is moved to and fro in front of the eyes. The checkered stripe is only seen when the single squares can be perceived separately. Otherwise, it does not stand out from the background and the movements of the board are not seen, as the edges of the board are hidden. Thus, the eyes of an observer will only follow the movements of the board if the checkered stripe is visible and it is only visible when the single squares are distinguished; hence the movements of the eyes are in close relation to the visual acuity of the patient observed.

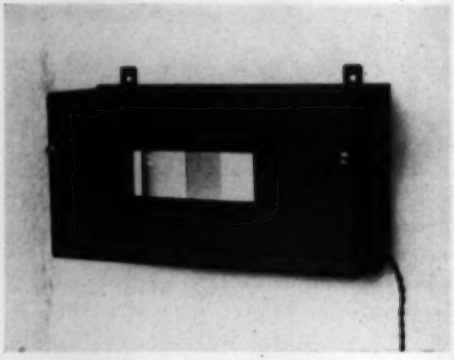

Fig. 1 (Schmidt). Equipment. In reality, the central perpendicular strip is invisible when its squares are invisible.

Description of the equipment (figs. 1 and 2)

The board with the checkered stripe measures 38 cm. by 15 cm., the horizontal side being longer. In the middle of it is the 6.2-cm. broad vertical stripe, composed of black and white squares, the sides measuring 1.15 mm. (fig. 2).

The outer sides of the board, right and left, are covered with 0.36-mm. squares. This fine pattern is perceived as a homogeneous gray field at a third of the distance needed to see the entire board as a homogeneous gray field. On the other hand, the actual stimulating field, that is, the coarse pattern of the stripe, only fades into the background at the greater distance. The printing of such a board is extremely difficult, since even trifling differences of brightness between stripe and background are clearly seen and movements can still be seen even when the squares are not distinguished. Small errors in the black intensity, however, have no optokinetic effect (Lüscher).

As already mentioned, the swinging board is situated behind a window 20 cm. in length and seven cm. in height which conceals the edges of the board from the observer. Above and below the window, on the back of the diaphragm, there are two Philips 40-watt candles, 28 cm. in length, which illuminate the test board uniformly with 1,800 lux.

No direct light from the bulbs can reach the eye of the observer. The amplitude of the board movement is 8.5 cm. The frequency of the to-and-fro movements of the board is 40 per minute. These are produced by a noiseless induction motor with crank

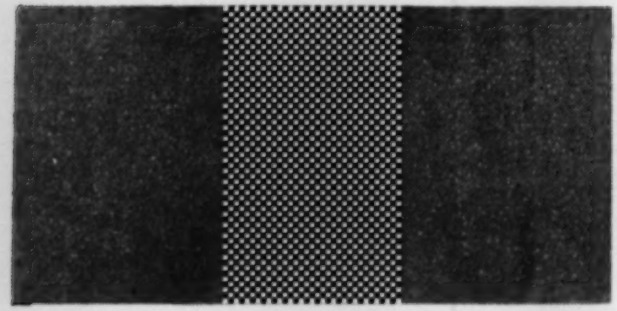

Fig. 2 (Schmidt). Testing board. If the board is correctly printed, then the checkered strip and its surrounding should appear uniformly gray when looked at from a distance at which the single squares are not perceived. As mentioned in the text, ordinary printing cannot fulfill this condition.

gear on rollers. The entire equipment is enclosed in a box 50.5 cm. by 26.5 cm. by 17.5 cm., fastened to the wall 125 cm. above the floor.

The optimal values of stripe size, window opening, frequency and amplitude of the movements, and illumination were determined by Pfister and Lüscher.

Theoretically, a person with a visual acuity of 1.0 should see the checkered stripe at rest from a distance of 3.80 m. The movement of the stimulating field and the fact that the checkered stripe has to induce optokinetic reactions which are correlated but not identical with threshold perception explain the empirical conclusion that, under our conditions of observation, a visual acuity of 1.0 (tested with Pflüger's E at 1,000 lux illumination) corresponds to the cessation of eye movements at 1.6 m. to 1.8 m. (fig. 3).

That the stimulating field is perceived as a whole and not as a sum of the squares has important consequences: the patient, who is often a malingerer, does not realize that the examination has anything to do with visual acuity, as the stripe he is looking at is large.

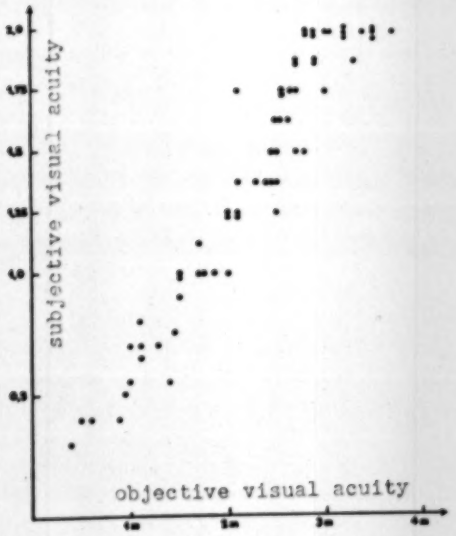

Fig. 3 (Schmidt). Correlation of subjective and objective visual acuity (Lüscher).

Generally, the person examined will, some seconds after looking into the window of the apparatus, make pendular eye movements in the rhythm of the swinging board. If the eyes do not move, which is unusual, even malingerers can be induced to move their eyes if told to follow the moving stripe with their eyes.

I would stress the fact that the movements of the eyes cease before any subjective perception of movements ceases. Hence, slight irregularities (clouds) of the swinging board do not interfere with the examination. There are very few people who cannot be induced to make eye movements in front of the swinging board.

The method can be employed between visual acuities of 0.1 and 2.0. Possible differences between results of objective and subjective examination vary between 1/10 and 2/10.

Examination procedure

Indications

A. Examination of the visual acuity by the subjective method for distance and reading.

B. Determination of refraction (retinoscopy, refractometry, after cycloplegics).

C. Routine eye examination.

D. Objective determination of visual acuity on the following day with narrow pupil.

Technique

1. The patient sits on a chair on casters immediately in front of the apparatus. Distance from patient to stimulating field approximately 30 cm. (12 inches).

2. If necessary, refraction errors should be corrected, possibly including presbyopia, corresponding to the initial distance and changing during examination with changes of distance.

3. The eye not to be examined is covered.

4. The patient is asked to look into the illuminated window of the box.

5. Movements of the eye are observed by

watching the conjunctival vessels with the electric ophthalmoscope equipped with a +20D. lens.

6. Wait for the movements of the eye, which generally occur after a few seconds. If spontaneous pendular movements of the eye cannot be elicited (which rarely occurs), the patient is requested to follow the moving stripe with the eye.

7. Distance between patient and stimulating field is gradually increased by means of the movable chair—the eye remaining under continuous control.

8. The distance at which the rhythmical movements of the eye cease is recorded. This will generally be after a few irregular nystagmic jerks (critical distance).

9. The distance is reduced until the rhythmical movements of the eyes recommence. Then there is a second increase of distance up to the critical point.

10. The average value of three tests is computed and the visual acuity is read from the calibration curve.

Generally, visual acuity of the apparently bad eye is examined first, but is—in every case—followed by the examination of the other eye. In the rare cases where neither eye shows any pendular movement, no conclusions can, of course, be made as to its visual acuity. In general, this method cannot be employed for the examination of aphakic eyes.

Summary

The final device and the method of objective determination of visual acuity after Goldmann are described.

Freiburgstrasse 8

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ELECTRICAL BURN OF RIGHT GLOBE AND ADNEXA

Isadore Givner, M.D.
New York

This case of an electrical burn in the region of the eye is presented because there was opportunity to observe it for six years, and because it illustrates the extreme degree to which the body itself can repair sloughed tissue.

The typical electric burn may result at the actual point of contact. The live terminal often leaves its imprint as a sharply defined necrotic mark without surrounding hyperemia. There is an absence of the immense swelling characteristic of the thermal burn. Generally the condition is painless. The heat generated is so intense and the dehydration of the tissue so complete that the subsequent slough separates with a sharp line of demarcation and heals by epithelization and granulation.*

Case report

On April 20, 1949, Mr. P. E., aged 38 years, fell on the third rail of the subway and hit the region of his right eye. The third rail carries 650 volts of D.C. current. The patient was knocked unconscious and when first seen later in the day both the upper and lower lids of the right eye had sustained a third-degree burn. No light perception was present in this eye. The lids were adherent to the globe. In the occipital region was an associated scalp burn. On May 4th, the cornea was sloughing, exposing the iris; both lids sloughed off (fig. 1).

* Duke-Elder, W. S.: Textbook of Ophthalmology. St. Louis, Mosby, 1954, v. 6 p. 6427.

Fig. 1 (Givner). Appearance two weeks after injury.

May 12th. An evisceration was done, cutting off the outer half of the globe. The inner contents of the globe were filled with blood. Vaseline packing was put in and the eye bandaged.

May 16th. Granulations were growing over the exposed right superotemporal portion of the malar bone. There was no periosteum present.

May 27th. The skin was growing in from all sides.

May 29th. New skin had completely grown in. The remnant of the conjunctival sac varied from 12 mm. vertically in some areas to six mm. in its nasal portion. The width was 24 mm. Both punctas were still intact (fig. 2).

In 1952, Dr. L. J. Feit made a new socket with a Thiersch graft. New brows were formed from the skin of the temporal region. New lids were formed from skin taken from the postauricular region. Today

Fig. 2 (Givner). Appearance two weeks after evisceration.

Fig. 3 (Givner). Final appearance.

the patient's appearance is as seen in Figure 3.

108 East 66th Street (21).

SUBJECTIVE REFRACTION OF DEAF MUTES*

PAUL W. MILES, M.D.
St. Louis, Missouri

For 18 months during the war, I served in an Army hospital attended by some Chinese civilians and Hawaiian troops who spoke no English. To save time in refraction, a simple sign language was developed which has since proved helpful for refracting deaf mutes. To my knowledge, such a subjective method of refraction has not been published.

One could, of course, refract these people as one does a small child, using retinoscopic and motility tests. However, the adult is not fully satisfied and would rather participate.

Just recently I refracted a deaf mute, aged 60 years, who has led an active useful life in clothing manufacture. He brought his daughter with him to serve as an interpreter of his manual speech. Much to their surprise, I finished the refraction in good time without asking the interpreter any questions or giving any instructions. The daughter told me that he had never had a satisfactory refraction before, because of

* From the Department of Ophthalmology and the Oscar Johnson Institute of the Washington University School of Medicine.

the lack of communication. He begged me to make my method known to other doctors.

The technique is quite simple, as it must be to avoid confusing the patient. Testing the visual acuity with the present glasses is done in the usual way by presenting isolated letters. The patient will either attempt to say the letter, or nod his head "yes." The same applies to tests of the near-point of accommodation with the old glasses on test type.

Next the room lights are turned off and the distant fixation light is flashed on and off to catch the patient's attention. Merely pointing at the light is enough to get the patient to hold fixation. It is easy to detect wandering fixation while using the retinoscope, because the pupil reflex becomes dull and the refraction inconstant. If fixation wanders, one needs only to point at the light again.

Lenses according to the retinoscopic findings are placed in the trial frame. The eye not being tested is occluded. Two trial lenses are held in one hand, +0.25D. and —0.25D. sph. The other hand is held about two feet in front of the patient's eyes so that one or two fingers can be presented as one shifts the —0.25D. (one finger) or the +0.25D. (two fingers) sph. before the eye. The patient is looking at a few letters on the 20/20 line, or at the smallest test type he can easily read as determined by the preliminary test. With no other instruction, the patient responds by presenting one finger or two, indicating which lens is preferred.

The fingers should be seen by the patient in a conspicuous place just below the test letters, but obviously not covering the letters. Since this sign language involves peripheral vision, small aperture lenses or the tubular refractor apparatus would not be satisfactory. Loose trial lenses of 23 mm. or more diameter work perfectly.

The method can also be used to compare no lens (one finger) with any lens, sphere or cylinder (two fingers). In effect, one is asking, "Is this better off (one finger) or on (two fingers)?" One could use the "fogging technique" in this way, but it would be slow compared to the primitive method described here. In those under the age of 40 years, one should do the first refraction under cycloplegic.

After the sphere has been determined, one should retest the cylinder power and axis by use of the Jackson crossed cylinder. For power, one presents less cylinder (one finger) and more cylinder (two fingers). Then for axis, one presents two alternatives with the two-finger signs. When the end point is reached for power or axis, the patient gestures "no-difference." This gesture comes in many forms, all intelligible. It is important to judge the effect of lens changes by observation of the patient's facial expression, as well as by the patient's hand gestures. For this reason, the trial frame is much superior to a refraction machine. If there is significant difference in the cylinder power, one should retest the sphere.

The habitual reading distance can be quickly determined by handing the patient a popular magazine or newspaper. Regardless of bad visual effects of incorrect lenses, a patient will at first place reading matter at the usual distance. One can only estimate the occupational working distance by direct questioning (pencil and paper). When astigmatism seems an important part of the refraction, I usually repeat the crossed cylinder tests at the reading distance. This can also be done by the sign language.

I have found it sufficient in deaf mutes to test heterophoria by the cover test, distance and near. Eye movements are then observed as the patient's eyes follow a small point of light. If the patient is intelligent, there is no waste of time in use of the Maddox rod test. Indicate the line with one index finger and the spot with the tip of the other. Bringing the finger tip to the "line," then jerking it emphatically at the moment of coincidence generally gets the idea across. Finger talk is easy for deaf mutes because they use it all of the time.

100 North Euclid (8).

OPHTHALMIC RESEARCH

Department

EDITED BY FRANK W. NEWELL, M.D.

Abstracts of papers presented before the Eastern Section of the Association for Research in Ophthalmology, April 28, 1956, at the College of Physicians and Surgeons, Columbia University, New York, New York.

IRVING H. LEOPOLD, *M.D., Secretary Eastern Section*

Serum protein changes in diabetic retinopathy. Sidney Lerman, M.D., and Burton M. Pogell, Ph.D., Wilmer Ophthalmological Institute, The Johns Hopkins University and Hospital, Baltimore.

Several investigators have postulated that disturbances in serum mucopolysaccharide metabolism occur in diabetic retinopathy, and that this derangement may have a primary relationship to the observed aneurysms. This has been examined experimentally by quantitative measurement of the different serum protein fractions by the technique of paper electrophoresis. Results were presented of the differences which appear in normal patients and in diabetic patients with and without retinopathy. A 15-percent increase in the α_2-globulin fraction was found in diabetics with retinopathy; whereas, there was no difference in the amounts of this fraction in normals and diabetic patients without retinopathy. The percent of total serum protein present in this fraction was 14.2 in diabetics with retinopathy, 12.3 in normals, and 12.0 in diabetics without retinopathy. The increase was statistically significant ($P<0.01$). This was the only protein fraction significantly increased in either diabetic group. The α_2-globulins have been reported to contain large amounts of mucoprotein.

These studies were extended to the changes which occur in the serum protein fractions in rabbits made diabetic by alloxan injection and in a similar group of rabbits given intramuscular cortisone acetate (8.3 mg. daily). In the alloxan-diabetic group, no significant change in the α_2-fraction occurred after four weeks. However, in the diabetic rabbits given cortisone, a marked increase of 17 percent wa found after one week which increased to 27 percent after three weeks. Since this level of cortisone is known to produce Kimmelstiel-Wilson kidney lesions in rabbits, it therefore appears that the increase in α_2-globulin fraction occurs simultaneously with capillary lesion formation in humans and rabbits.

Preliminary report on studies with anti-lens antibodies. S. P. Halbert, D. L. Khorazo, P. Fitzgerald, L. Swick, B. Seegal, R. Witmer, and G. Smelser, College of Physicians and Surgeons, Columbia University, New York.

Antisera against adult rabbit lens have been prepared in adult rabbits, with the aid of Freund's adjuvants. By the use of agar precipitin technique, it has been shown that up to five rabbit lens components may induce antibody formation. Evidence was obtained that one of these antigens is lacking in detectable amounts in 26-day-old fetal and newborn rabbit lens. This antigen seems to make its appearance between 10 and 19 days post partum.

The cross reactivity of these homologous rabbit lens antisera with the lenses of other species has been studied. The strong cross reactions with other mammalian lenses (organ specificity) is due to

the similarity of antigenic structure of from three to five of these components. With a strong homologous rabbit lens antisera, cross reactions have been found with two components of frog lens, and one of a salt water fish lens (menhaden). In an extension of these observations, antisera (in rabbits) have been prepared against fish and frog lens, also with the aid of adjuvants. Frog lens antisera have shown five components with frog lens and fish lens antisera have shown four components with fish lens. Frog lens antisera may show four, while fish lens antisera may show three antibodies cross-reacting with adult rabbit lens.

Attempts are underway to isolate and identify the antigens involved, by means of continuous flow electrophoresis of the various lens homogenates.

Effect of age upon lens metabolism. H. Green, S. A. Solomon, and Irving H. Leopold, Wills Eye Hospital, Philadelphia.

Establishment of the Embden-Meyerhof scheme as the basic pathway of anaerobic carbohydrate metabolism in the young rabbit lens (Green, Bocher, and Leopold) made it desirable to determine whether physiologic aging of the lens is accompanied by disruption of the sequence of enzymatic events. Such information might lead to a better understanding of the pathogenesis of senile cataract. The metabolic activity of young rabbit lens relative to the catabolism of carbohydrate was compared with that of old rabbit lens under the optimal conditions. The results show that the capacity of the lens to produce lactic acid from glucose or from intermediary metabolites is apparently not diminished with aging. When calculated on the basis of dry weight or the weight of protein, however, the metabolic activity of the older lens is quite markedly lower than that of the younger lens.

Oxidation of thiolic groups of lens proteins by heavy metal in presence of inorganic phosphate. Alain Croisy and Zacharias Dische, Department of Ophthalmology, College of Physicians and Surgeons, Columbia University, New York.

The formation of albumoid during the life span of animals and humans has been shown to be due to an oxidation of thiolic groups of soluble lens proteins. In studies on the proteins of rat lenses, however, no significant amounts of cystine could be found in soluble lens proteins. In lenses of young rats, on the other hand, the presence of a protein was demonstrated which on oxidation becomes insoluble. The amount of this protein decreases sharply with the age. These findings suggested that in adult animals a specific protein is present in small amounts which is oxidized to a greater extent and faster than the main bulk of proteins.

To test this possibility, the beta crystallin fraction of ox lenses was fractionated by salting out with a mixture of $KHPO_4$ and Na_2HPO_4 at pH 6.5. Derrien and Jayle obtained by this procedure six different fractions of beta crystallin. Four different fractions were prepared which precipitated between 1.4 and 2.2 M phosphate. A fraction representing about 10 percent of the total beta crystallin remained in solution at 2.2 M and precipitated after the salt was dialyzed out.

Cysteine and cystine were then determined in all these fractions and compared with the amounts of cysteine found in original beta crystallin preparation. Significant amounts of cystine were present in all fractions; the fifth fraction which did not precipitate even at 2.2 M of phosphate contained only cystine and no significant amounts of cysteine. This indicated an oxidizing effect of inorganic phosphate on beta crystallin and the presence of one small fraction which is much more susceptible to this oxidation than the rest of proteins.

Further experiments on soluble proteins of rat lenses showed that the thiolic groups of these proteins are significantly

oxidized in phosphate buffer at pH 7.4 at 38°C. in two and one-half hours, even at as low concentrations of phosphate as M/15. The oxidative ability of inorganic phosphate is due to the formation of heavy metal complexes. These experiments demonstrate the presence of a non-enzymatic system in the lens which is able to catalyze the oxidation of thiolic groups of proteins.

Studies with an antibiotic from an ocular staphylococcal strain in gas gangrene infections of mice. S. P. Halbert, C. Kazar, and L. Swick, College of Physicians and Surgeons, Columbia University, New York.

Previous studies have demonstrated that antibiotic production by micro-organisms of the normal ocular flora is extremely common. In experimental mixed infections with such organisms in mouse gas gangrene, it has been demonstrated that such antibiotic producing strains can protect against many lethal doses of Clostridium septicum spores, while nonantibiotic producers are without effect. These studies indicated that the mechanism of protection in such mixed infections was through the in vivo production of the antibiotics by the staphylococcal strain. Partially purified antibiotic concentrate of high potency has now been obtained from one of these ocular staphylococci (with the co-operation of Eli Lilly & Co.). It has been demonstrated to be distinct from other known antibiotics. The concentrates are of very low toxicity for mice and have been shown to be of very great effectiveness in the prophylaxis and early therapy of mouse gas gangrene (Cl. septicum). These data constitute almost conclusive evidence that the protection previously obtained in mixed infections is, in fact, mediated through the in vivo production of antibiotic in the tissues. In addition, they strongly suggest that the normal bacterial flora of humans may present a very fertile field for the search for new antibiotics of limited spectra.

The agar-diffusion technique as applied to the detection of anti-Toxoplasma precipitins in aqueous humor. G. Richard O'Connor, M.D., National Institute of Neurological Diseases and Blindness, Ophthalmology Branch, Bethesda, Maryland.

An attempt has been made to arrive at a specific diagnosis of ocular toxoplasmosis by immunologic means.

In a preliminary experiment, the presence of precipitins in the sera of rabbits and humans having known high Toxoplasma dye test titers was demonstrated by the standard serial tube-dilution method using antigen prepared from the peritoneal exudate of Toxoplasma-infected mice. Gamma-globulin fractions of high purity were prepared from these same human and rabbit sera using the electroconvection apparatus of Raymond, et al. at pH 7.5. Using this material as antibody and a 1:10 dilution of the supernatant fluid from mouse peritoneal exudate as antigen, agar-diffusion plates were set up after the manner of Ouchterlonie, as modified by Halbert. The medium consisted of 0.7-percent Bacto-Agar to which sodium barbital and glycine were added to final concentrations of M/25 and M/20 respectively. The molten agar was adjusted to pH 7.4 with concentrated HCl. Wells or reservoirs were cut out of the agar using sterile cork-borers and were arranged in a hexagonal pattern around a larger central well at a radial distance of 1.3 cm. Precipitin lines were formed in the agar at right angles to a line drawn between the centers of the antibody and antigen wells. Using undiluted gamma globulin (0.62 mg. protein N per ml.) these lines appeared at about 48 hours (at 7° C.)

Employing exactly the same technique, aqueous humor samples obtained by paracentesis from patients with granulomatous uveitis were placed in the center wells of similar agar plates. These samples (0.15 ml. of undiluted fluid) were heated for one hour at 56°C. prior to use.

Various antigen solutions were pipetted into the peripheral wells, including: supernate from the peritoneal exudate of Toxoplasma infected mice; a control antigen made of noninfected mouse tissue; erythrogenic beta-hemolytic Streptococcus; Staphylococcus; Histoplasma; Coccidioides; and purified protein derivative of M. tuberculosis.

In three patients with suspected ocular toxoplasmosis, having serum dye-test titers ranging between 1:2,024 and 1:232,116, characteristic precipitin lines were obtained using aqueous humor specimens and Toxoplasma antigen. This finding was correlated with Toxoplasma dye test titers in the aqueous humor of 1:16 to 1:32. Two of the three patients had moderately severe anterior uveitis as well as chorioretinitis. Another patient with a posterior pole lesion alone, and a negative aqueous dye test, showed no precipitins. Still another patient with probable tuberculous uveitis showed no precipitins. If subsequent protein fractionation studies of blood and aqueous reveal that there is relatively more antibody in the anterior chamber than could be accounted for on the basis of permeation of the blood-aqueous barrier, it is felt that this method of testing will have great diagnostic value in the etiologic evaluation of uveitis.

The inflammatory response of the eye to injected erythrocyte stroma. David H. Rhodes, Jr., M.D., Institute of Ophthalmology, Columbia University, New York.

During the course of studies on the absorption of experimental vitreous hemorrhages in rabbits, an unexpected inflammatory response was noted when hemolyzed erythrocytes were injected into the vitreous. Further investigation showed that hemoglobin was completely inert when injected, but that the ghosts of the erythrocytes provoked a marked inflammation. The erythrocyte stroma was further fractionated by extracting the lipids and at least part of the polysaccharides, and injecting the extract and the residual protein separately. Preliminary results indicate that the extracted lipid and polysaccharide fraction is not toxic while the residual protein induces a severe endophthalmitis. Cultures of the injected suspensions and of the eyes revealed no bacterial contamination. Each rabbit received injections of fractions of its own blood, eliminating possible cross-reactions from different blood groups.

Clinically most of the eyes which received injections of the erythrocyte stroma in the early series and of the protein fraction in the later series showed a severe endophthalmitis which progressed to phthisis bulbi. One eye which did not react so violently to the injection of ghosts subsequently developed vitreous bands and a retinal detachment, while two eyes which had been injected with hemolyzed blood containing ghosts developed typical retinitis proliferans.

These observations raise the possibility that in massive vitreous hemorrhages or in repeated hemorrhages, chronic irritation from the toxic factor in the red cell stroma may, in part at least, stimulate the development of vitreous bands and of retinitis proliferans. Further studies to identify the toxic portion of the stroma are in progress.

Plasma steroids after intravenous typhoid vaccine. Anthony Donn, M.D., and Nicholas Christy, M.D., Departments of Ophthalmology and Medicine, Presbyterian Hospital, New York.

In 14 patients with various ophthalmologic disorders, the administration of intravenous typhoid vaccine (5 to 15 million killed organisms) caused a sharp rise in plasma 17-hydroxycorticosteroid levels as measured by the Silber-Porter technique. The peak corticosteroid levels coincided closely with the maximum temperature increase and were comparable to levels attained after standard intravenous

ACTH tests (36 to 59 μg. percent). An attempt was made to determine whether this adrenocortical stimulation depended solely on the febrile response to typhoid, or could be produced in the absence of fever. Since it is known that the administration of aminopyrine inhibits the febrile response but does not prevent certain hemodynamic effects characteristic of the pyrogenic reaction (Bradley, S. E., et al.), the drug was given to three patients over the 24-hour period prior to the typhoid dosage. The febrile reaction was suppressed. No rise in plasma 17-hydroxycorticosteroids occurred, although the drug failed to abolish other systemic effects of the vaccine (weakness, nausea). It is concluded that aminopyrine action on the central nervous system, by blocking the pyrogenic effect of the typhoid vaccine, prevents the stimulus to ACTH-release and hence to adrenocortical activation.

Observations on pupillary dilator muscle activity. Otto Lowenstein, M.D., and Irene E. Lowenfeld, College of Physicians and Surgeons, Columbia University, and the Institute of Ophthalmology, Presbyterian Hospital, New York.

Anatomic existence of radial muscular fibers in the iris is today generally accepted. But the physiologic role of the dilatator pupillae remains a subject of controversy. Some authors believe that its active contraction contributes the main force to pupillary dilatation. Others maintain that pupillary dilatation is primarily or entirely caused by relaxation of the sphincter muscle; they attribute to the dilatator the role of a "tonic counter-balance" which passively adapts itself to the motions of the pupillary sphincter.

One of the main arguments brought forth in support of the latter theory is based on the fact that isolated sphincter strips, suspended in warm Ringer's solution, relax when adrenalin is added to the solution. This behavior is supposed to prove that the sphincter muscle is supplied not only by cholinergic constrictor fibers from the oculomotor nerve, but also by adrenergic inhibitory fibers running over the cervical sympathetic chain.

Experiments were made on the iris of cats, dogs, and rabbits. Portions of the sphincter were separated from the rest of the iris by circular cuts. The spontaneous behavior of these preparations as well as their pharmacologic reactions and responses to electrical stimulation were observed. Based on these experiments, it was shown (1) that an active radial dilator force exists in the iris and (2) that adrenergic relaxation of the sphincter muscle is not the cause of pupillary dilatation, though it may possibly facilitate the motion.

The clinical value of the Rodenstock refractometer. Frank I. Hobbs, M.D., and Robert A. Schimek, M.D., Department of Ophthalmology, Henry Ford Hospital, Detroit.

An evaluation of the accuracy and practicality of the Rodenstock refractometer in a large clinic practice was based on a comparison of this objective method with the customary subjective methods of manifest and cycloplegic refraction. A total of 479 eyes of 242 patients was studied, representing the refraction of 1,226 eyes by the three different methods. The results were recorded in graphic form to show the deviation of the noncycloplegic Rodenstock determinations from the customary manifest cycloplegic refraction. The results show acceptable accuracy of the Rodenstock refractometer compared to the subjective methods. The graphs reveal good conformation to the standard deviation curve. The study also indicated that, when used by an experienced technician, the method produced less error, due to accommodation, than the average manifest refraction as compared to the subjective cycloplegic refraction.

Observations on treatment of an experimental fundal tumor, and a new approach to embryonic carcinogenesis. Adolph W. Vogel, Michael Kaczurowski, Khalida Naib, and Irving H. Leopold, Wills Eye Hospital, Philadelphia.

Rabbit squamous cell carcinomas (V-2), transplanted into the fundus of rabbit eyes, were treated with the Stallard disc, cautery, and chemotherapy. It was found that the Stallard disc destroyed all cells within its periphery of 3,500 + r. Adjacent tumor tissue was sometimes but not always destroyed. This may depend on the inherent resistance of the individual host. Cautery, as used, showed no difference between the treated and untreated eyes. Chemotherapy plus cautery showed slight improvement in the response of treated cases. In the doses used of HN2, TEM, and colchicine there were indications of a damaging effect to the retina when given intra-arterially.

Intraocular pressure and eye growth. Alfred J. Coulombre, Ph.D., Yale University School of Medicine, New Haven, Connecticut.

Short lengths of microcapillary glass tubing were introduced into the vitreous body through minute incisions in the eye walls of chick embryos at four days of incubation. Such tubes were left in place and allowed egress of vitreous humor and lowered intraocular pressure. The equatorial diameter of such eyes was measured at daily intervals for four days following the operation. These eyes showed virtually no increase in size over the four-day experimental period, whereas the contralateral, unoperated eyes showed the sevenfold increase in diameter normal for this period. Similarly, the corneas of operated eyes showed little increase in diameter over the four-day period, whereas the corneas of unoperated eyes underwent a threefold increase in diameter.

To control trauma and other nonspecific factors, operations were performed as above except that solid glass rods were utilized. The glass rods did not allow the escape of vitreous humor. In these cases the eye grew normally with respect to the equatorial and corneal diameters.

The results suggest that intraocular pressure is a cardinal factor in the growth of the vertebrate eye.

Reparation of the fetal eye following X-irradiation. Roberts Rugh, Ph.D., and Miss Joan Wolff, Radiological Research Laboratory, Columbia University, New York.

One of the possible hazards sequential to whole body X-irradiation is damage to the eyes. It seems evident that neutron exposure is more conducive to ultimate cataract development than are X rays, although such a generalization cannot be made for all classes of animals. Realizing that the fetal tissues are more radiosensitive than are those of the adult, a study was made of the effect of tolerable exposures of the fetal mouse to X rays on the neurectoderm and neuroblasts of the developing retina.

Pregnant mice were exposed to whole body X rays on gestation days 12.5 and 13.5 (when the eye is actively differentiating) and the doses ranged from 50 r to 300 r in single exposure. At four, 24, and 72 hours thereafter, at birth and again at two months, eyes of such mice were studied histologically and cytologically.

Previous studies of this nature have been based largely upon the condition of the eyes at birth. Such studies did not reveal the remarkable reparative powers of the fetal retina.

At four hours postirradiation and at the higher levels of exposure there was extensive retinal damage with approximately half of the retinal neuroblasts reduced to fragmented masses of cytoplasm and nuclei. Many nuclei were pyknotic or karyorrhectic. Both the inner and outer nuclear zones were involved. Most of the dead cells were already sloughed off into

the vitreous body or between the retina and the pigmented layer. Such fetal eyes appeared to be beyond repair. However, 24 hours following X-irradiation there was still evidence of further damage (probably to cells which attempted mitosis) but there was extensive phagocytosis, so that some of the extraretinal debris was being removed. By 72 hours after exposure the retina appeared to be quite normal and there were only scattered clumps of dead cells and nuclei yet unremoved by the active phagocytes.

At birth the eyes appeared to be normal histologically and at two months they were definitely functional, although the degree of visual acuity was not determined. However, if one measures these eyes it is evident that those which were exposed to 150 r at 12.5 days gestation were reduced in volume to 70 percent and when the exposure had been 250 r the volume reduction was to 51 percent. Thus, both doses resulted in some degree of microphthalmia, and reparation was therefore quantitatively incomplete.

While the fetal eye of the mouse is extremely radiosensitive, due to the presence of neuroblasts, it exhibits remarkable powers of repair and reconstitution. This is due to the efficient removal of the irradiation-damaged nuclei and cells and their replacement from undifferentiated neurectoderm cells. There is no evidence of "recovery" of the irradiation-damaged nuclei and cells. Such eyes are microphthalmic to a degree related to that of X-irradiation. The eyes are functional but whether their visual acuity is entirely normal has not been determined.

Growth of glutamotransferase in the retina of the developing chick. Dorthea Rudnick, Ph.D., Department of Biology, Albertus Magnus College, New Haven, Connecticut.

Investigation, jointly with H. Waelsch, of the course of development of the enzymatic activity designated as glutamotransferase in nervous tissue of the chick embryo has shown that this enzyme is not appreciably active in the central nervous system until halfway through incubation. During the latter half of incubation (after about 10 days) the specific activity, tested in fresh homogenates, rises gradually to about unity in all parts of the brain, with only slight divergences in rate between various parts. The retina does not share this enzymatic development. Instead, its glutamotransferase activity remains minimal until about the 17th day of incubation. At this time a rapid rise in specific activity takes place, continuing until some days after hatching, when specific activities as high as six are reached.

At present, this history seems best interpreted by assigning to some definite cell type or types in nervous tissue a special glutamotransferase activity, increasing just before and just after hatching as one aspect of functional maturation. A start has been made in analysing the contribution of local factors to the rise in activity of the retina. Optic cups, with corneal and lens primordia, from embryos of approximately two days' incubation, have been transplanted to the flank or yolk sac of host embryos of similar stages. In favorable cases the graft develops into an eye of size and gross form quite comparable to the unoperated control. In such eyes, the retina appears to be very accurately and normally differentiated, except that the ganglionic and optic fiber layers are either absent or very much reduced. The glutamotransferase activity of these retinas, however, does not fall outside of the normal range for unoperated eyes of comparable age.

It must be concluded that the rise in glutamotransferase activity cannot be dependent on local vascular conditions or on actual visual function. Furthermore, it is clear that the ganglionic cells do not contribute differentially to the glutamotransferase activity and that their functional maturation cannot be the occasion of the

spectacular increase of this activity in the retina at hatching.

Hue discrimination and luminous efficiency for the normal and deuteranopic eye of a unilateral color-blind subject. Yun Hsia, Ph.D., and C. H. Graham, Ph.D., Columbia University, New York.

Screening tests seem to indicate that one eye of a young woman whom we have examined is deuteranopic and the other eye normal.

The luminous efficiency for the deuteranopic eye is lowered in comparison with that of the normal eye for wavelengths shorter than 530 mμ. This loss is comparable to that of a group of binocular deuteranopes contrasted with normals.

The hue discrimination curve for our subject's color-blind eye shows a major minimum near the neutral point, 500 mμ. In addition two other minima appear: one near 420 mμ and the other near 660 mμ. Thresholds for the normal eye showed conventional minima. Binocular color comparisons indicate that the color blind eye can see blue, yellow, violet, and pink. This result is not in accord with classical concepts.

Color mixture data show that the normal eye of our subject requires three primaries to match a narrow spectral band, while the deuteranopic eye requires only two.

Binocular brightness matches of a unilateral color-blind subject in various spectral regions. E. Berger, Ph.D., C. H. Graham, Ph.D., and Y. Hsia, Ph.D., Columbia University, New York.

Experiments have been performed to determine whether the selective spectral luminosity losses manifested by the color-blind eye of a uniocular deuteranopic subject at threshold would be maintained at high photopic luminance levels. The subject was a young woman with typically normal color vision in the right eye and essentially deuteranopic vision in the left eye.

Binocular brightness matches between two fields, each subtending 1.8 degrees of visual angle, were made by means of a polarization type of photometer. Determinations extending over a luminance range of approximately three log units were made for each of eight spectral regions between 450 and 608 mμ, the color of the light being controlled by appropriate color filters.

For a report of apparent equality of brightness of the two binocularly viewed test fields, the luminance requirements for the field seen by the subject's color-blind eye exceed those for the field viewed by her normal eye in the blue, blue-green, green, yellow-green, and yellow portions of the spectrum; they are identical in the red end of the spectrum, where apparent equality of brightness is identical with physical equality. The loss of luminance for the deuteranopic eye is greatest in the green and least in the yellow, the blue loss being intermediate between these two. Furthermore, these selective spectral luminosity losses are maintained over the luminance range tested.

The results are interpreted as confirming the existence of the selective spectral luminosity losses previously found at threshold for the color-blind eye of this subject. Their bearing on the possible mechanism responsible for color blindness, as well as their implications for theories of color vision in general, was briefly considered.

Physiologic variations of bicarbonate ion concentration in the intraocular fluids. H. Green and Irving H. Leopold, Wills Eye Hospital, Philadelphia.

According to currently accepted theory bicarbonate ion is considered to be actively transferred from the blood plasma into the aqueous humor as a result of cellular metabolic activity of the ciliary processes.

Very little is known, however, of the

functional dependence of the active transfer mechanism upon the plasma bicarbonate level. This investigation was therefore initiated in order to determine the relationship between the fundamental capacity of the active transfer of bicarbonate ion concentration with the plasma bicarbonate level. Rabbits were continuously infused intravenously with isotonic or hypertonic sodium bicarbonate and the bicarbonate ion concentration in the anterior chamber, posterior chamber and vitreous humor were compared with that in the plasma under steady-state conditions over a period of five hours.

The results show that when the blood bicarbonate is raised to a level of 30 mM/l within 60 minutes and by the intravenous administration of 1.3 percent $NaHCO_3$ maintained constant for the next four hours, the bicarbonate ion concentration of the anterior chamber aqueous humor rose to a level of 35 mM/l in 60 minutes, and remained constant for the next two hours, and then fell during the final two hours to a value of 32 mM/l. The bicarbonate ion concentration of the posterior chamber aqueous humor, on the other hand, increased in 60 minutes to a level of 43 mM/l and after the second hour, showed a tendency to rise slowly during the next three hours to a level of 45 mM/l. The distribution of HCO_3^- in the vitreous humor of normal rabbit eyes was: area adjoining the ciliary body, 31.3 mM/l; the remainder, 24.0 mM/l. After five hours of intravenous infusion of 1.3 percent $NaHCO_3$ concentration of the vitreous around the ciliary body did not change, while that in the rest of the vitreous increased to 26.5 mM/l.

Chemical composition of aqueous humor and vitreous body of different animal species. Endre A. Balazs, M.D., Retina Foundation, Boston.

The chemical composition of the vitreous body, with special regard to the hexosamine, hexuronic acid, protein nitrogen, hydroxyproline, and ascorbic-acid content, was studied in different animal species. Birds, such as chickens, turkeys, and pigeons, have a very low hexuronic acid content (less than 10 µg per ml.) in the vitreous body, suggesting that the hyaluronic-acid content of the vitreous body of these animals is less than 20 µg per ml. The hydroxyproline content of the gel vitreous of birds is 20 to 30 µg per ml., while in the liquid vitreous, it is only 0.2 to 0.6 µg per ml.

Cod, sunfish, and shark vitreous was also studied, and there the hexuronic acid and hexosamine content indicated a hyaluronic acid content of 70 to 100 µg per ml. The hydroxyproline content was highest in cod (52 µg per ml.). Squid vitreous is a liquid, with an estimated hyaluronic acid content of 200 to 300 µg per ml. Practically no collagen was found in the vitreous of this animal. The vitreous of rabbits seven weeks to two years old showed a rather uniform hexuronic acid content of 10 to 16 µg per ml. The hydroxyproline content in these animals was 14 to 18 µg. per ml.

The ascorbic-acid content of the analyzed bird vitreous and fish vitreous was less than 20 µg per ml. The ascorbic acid content in the vitreous of all mammals investigated was 10 times higher.

The aqueous humor of sunfish, fowl, rabbits, and cattle was studied with special regard to a possible mucopolysaccharide content. No appreciable amount of hexosamine or hexuronic acid was found in any of the animals investigated. Electrophoretic studies on cattle aqueous support this finding.

Pathology of the angle of the anterior chamber in primary glaucoma. A. L. Kornzweig, M.D., the Medical Service, The Home for Aged and Infirm Hebrews, New York. This work was supported by a grant from the United States Department of Health, Education, and Welfare (B-154).

Eleven eyes, obtained postmortem from seven patients with primary glaucoma were examined for changes in the angle of the anterior chamber. All were treated medically while the patients were residents of the home and hospital, and none had had ocular surgery. The positive pathologic findings in the angle were:

1. Thickening and sclerosis of the trabeculae.
2. Narrowing or obliteration of the intertrabecular spaces.
3. Variation in the patency of the canal of Schlemm from narrowing and partial occlusion to complete occlusion.
4. Endothelial proliferation causing occlusion of Schlemm's canal.
5. Pigment granules and cells in varying amounts in the intertrabecular spaces.

A study of temporal aspects in the human scotopic electroretinogram. Hans Bornschein, M.D., National Institute of Neurological Diseases and Blindness, Ophthalmology Branch, Bethesda, Maryland.

The relationship between the implicit time (interval from onset of light stimulus to peak of wave) and the amplitude of the scotopic b-wave in the human electroretinogram was studied while varying the wavelength and intensity of the light stimulus.

The experiments were made in three normal subjects, and the results were checked by records from a total color-blind and a congenitally night-blind subject. The absence of the photopic component was controlled by flicker electroretinography. The results are based on 618 records and given as mean values of six to 12 individual records taken under the same experimental conditions.

With increasing stimulus intensity, not only does the amplitude of the b-wave increase but the implicit time decreases. The range of implicit time is limited by a maximum of 120 to 140 milliseconds and a minimum of 60 to 70 milliseconds. There is a definite correlation between the amplitude and the implicit time of the b-wave, irrespective of the wavelength producing it. This correlation can be expressed in mathematical terms by a simple exponential equation.

From these results the conclusion can be drawn that the variation of the implicit time observed by some authors is an inherent property of the b-wave, and cannot be explained solely on the basis of a participation of the more rapid photopic x-wave in the complex response. Furthermore, the influence of colored light stimuli on the implicit time of the b-wave is related to stimulus intensity, and not to a specific effect of wavelength. Finally, the results obtained from normal color blind, and night blind subjects prove that the "late positivity" interpreted by Auerbach and Burian as a specific red response is actually the scotopic b-wave.

Mechanical pellet injector for carcinogens. Michael Kaczurowski and Adolph W. Vogel, Wills Eye Hospital, Philadelphia.

A perforator-ejector for pellets of carcinogen or any compressible compound has been developed for the implantation of carcinogens into the chick embryo eye, eye and brain of newborn mice, guinea pigs, rabbits, and rats. Embryonic and newborn structures are too delicate to permit surgical manipulation. This instrument overcomes the difficulty by using a spring mechanism which drives a perforating needle into the selected structure and ejects a contained pellet.

SOCIETY PROCEEDINGS

Edited by DONALD J. LYLE, M.D.

NEW ENGLAND OPHTHALMOLOGICAL SOCIETY

February 16, 1955

DR. FRANK W. DIMMITT, *presiding*

At the afternoon session several interesting clinical cases were presented for observation and discussion, and Dr. C. B. Favour of Palo Alta Medical Research Foundation, Palo Alto, California, presented a paper on "Bacterial allergy of the eye."

At the evening session, a paper entitled "An immunologist's approach to problems of ocular allergy" was presented by Dr. Byron H. Waksman, associate bacteriologist of the Massachusetts General Hospital, and an associate in bacteriology and immunology at the Harvard Medical School in Boston. The abstracts of the papers follow:

BACTERIAL ALLERGY IN THE EYE

DR. C. B. FAVOUR introduced his clinical material with a review of the current status of experimental work on bacterial allergy. It was pointed out that there are two basic types of allergic reactions—the immediate type which includes such phenomena as hives, bronchospasm, purpura, and the Arthus reaction, and the delayed type which is best illustrated by the tuberculin reaction. Bacterial allergy includes both types of reaction, but is most often identified with the delayed type of tissue damage.

It was emphasized that immediate-type allergy is associated with circulating antibodies, whereas delayed-type allergy is associated with cells of the lymphoid and reticulo-endothelial system. Tissue changes following immediate allergy are usually evanescent. Those associated with delayed allergy often lead to severe tissue damage with healing by scar tissue formation.

A classification of infectious eye disorders by allergic type includes three basic groups. Few conditions are pure forms. Seasonal hay-fever blepharitis is a classical example of immediate-type allergy in the eye. Iritis is a good example of bacterial allergy. A granulomatous uveitis, in which the parasite itself is in the eye, where it leads to either or both types of allergic response, as well as to local granuloma formation, is the third category of eye disease. The variable degree of isolation of these lesions within the eye from an allergic and immunologic viewpoint complicates their eradication by the host and by doctors' ministrations.

A clinical evaluation of 35 patients with bacterial eye disease was presented. An epidemiologic, physical, bacteriologic, and immunologic examination, using a battery of bacterial skin tests, was carried out. It was found that a history of other manifestations of allergy was of the same frequency as that in the general population. Acute dental infections coincident with eye disease were present in eight persons. All but two edentulous persons had some form of recurrent dental infection. Chronic bronchial infections were present but not directly correlated with eye symptoms in two subjects. Chronic empyema was correlated with eye symptoms in one patient. Chronic prostatitis was correlated with eye symptoms in two patients. Chronic infection in the gastrointestinal tract was correlated with eye symptoms in two patients. One patient only was suspected of having tuberculosis as the cause of his eye disease. One patient was suspected of having brucellosis as the cause of his eye disease. Three subjects were suspected of having a B. hemolytic streptococcus infection as a contributing cause to their eye disease. No obvious clue was found in 10 subjects. Of the group remaining, two had rheumatoid arthritis of mild degree. Ten of

the total group gave a past history of acute, nondeforming arthritis lasting a month or more.

Staphylococcus aureus was recovered from the eyes of patients with conjunctivitis and recurring superficial corneal ulcers. It was also found in the prostatic secretions of those with prostatitis. Bacterial skin tests showed that patients in this series often have significant delayed-type allergy to the streptococcus family. When other organisms were the likely cause, skin tests with appropriate materials showed significant reactions to these testing substances. Patients showed many fluctuations in their reactivity to test substances. Sometimes the increases correlated with infection, sometimes they did not. There was significant skin reactivity present to one or more bacterial agents in all the patients studied. The only exceptions were those with conjunctivitides and superficial corneal ulcers. These subjects reacted similarly to normal healthy controls.

Beyond the standard measures of cortisone and various eyedrops for acute manifestations of bacterial eye disease, two principles of management of these patients were suggested:

First, remove the source of infection. This was attempted with penicillin in the B. hemolytic streptococcus infections; while in use, it blocked recurrences. Reinfection was a problem. Removal of infected teeth and the control of bowel and prostate infection in others were effective.

The second principle was to desensitize the host, if removal was not possible. This succeeded once with old tuberculin for suspected tuberculosis and many times in the control of staphylococcus infections. Half of the patients with staphylococcus conjunctivitis responded to vaccine treatment. No patient of four treated with B. hemolytic streptococcus vaccine, and of six treated with alpha hemolytic streptococcus vaccine, responded to treatment.

The number of times significant infection was found and its treatment was possible, although small, was enough to justify a similar management of these types of eye problems in the future.

Discussion of this paper was very spirited and consisted primarily of various members of the society recounting individual cases which, in their experience, would bear out Dr. Favour's observation that focal infection does indeed seem to play some part in the background of certain ocular disorders.

Immunologic approach to ocular allergy

Dr. Byron H. Waksman said that hypersensitive reactions were divided into five clearly distinguishable categories: (1) Immunohematologic diseases; (2) immediate reactions, including anaphylaxis, atopic allergy, and the wheal and flare (local-cutaneous anaphylaxis); (3) "early" (compared with delayed) or "late" (compared with immediate) reactions, including the Arthus reaction and possibly arteritis of the periarteritis nodosa type; (4) tuberculin-type or bacterial allergy; and (5) contact allergy. Other inadequately characterized categories of reaction may exist.

1. *The immunohematologic diseases* result from damage to red cells, white cells, or platelets when antigen and antibody combine in or on the cell surface, with or without the participation of complement. The antigen may be a normal or altered constituent of the cell surface or an adhering substance such as a drug.

2. *Immediate reactions.* These diseases provide a good model for understanding events in anaphylaxis. Here antibody apparently adheres to the cell, and the damaged antigen-antibody combination results in release of pharmacologically active substances. The substances released, in particular histamine, heparin, and choline derivatives, account quantitatively for most of the symptoms of anaphylaxis. The source of these agents may be mast cells in some species,

platelets in others (rabbit). The wheal and flare is the same phenomenon elicited locally.

Atopic allergy appears to depend on identical physiologic mechanisms. The familial incidence of atopy has been shown to depend on an unusual proneness to produce sensitizing antibody in response to poor antigens. Its localization in a "shock organ" is as yet incompletely explained. The atopic patient given antigen intravenously develops typical anaphylaxis.

3. *The Arthus reaction* in the skin appears to depend on an entirely different process. While precipitating antibody can passively produce both Arthus sensitivity and anaphylactic sensitivity, nonprecipitating antibody can only produce the latter. Antisera produced by horses, cattle, rats, or birds produce Arthus sensitivity but not anaphylactic sensitivity. The amount of antibody required for an Arthus reaction is of the order of 1,000 times greater than is needed for an anaphylactic response. There is no evidence that antibody must be fixed in the tissues for the Arthus reaction, unlike anaphylaxis (several types of experiments). Histamine need not participate in the production of a typical Arthus. And finally the time course and histology of the two types of reaction are quite different. The Arthus mechanism appears to depend on the mechanical consequences of the formation of an antigen-antibody precipitate in some relation to vessel walls. Since a characteristic periarteritis can be produced passively with precipitating antibody-antigen systems, periarteritis nodosa may be tentatively assigned to the same category of hypersensitive reactions as the Arthus.

4. *Tuberculin-type sensitivity* (often called "delayed" hypersensitivity) is present in many infections, particularly granulomatous processes such as tuberculosis, syphilis, brucellosis, and so forth, and undoubtedly plays a major role in the evolution of the infectious lesion. The skin response has a characteristic time course and an histology distinct from the other reactions discussed.

The following experimental points distinguish this type of hypersensitivity from those previously mentioned:

The typical sensitivity can be produced only by injecting the antigen with special adjuvant materials, for example, the lipopolysaccharide of the tubercle bacillus, or, at least, in certain cases, by special routes (intradermally in small doses).

No circulating antibody has been shown to have any relationship to tuberculin-type sensitivity; indeed passive transfer can only be accomplished with living cells, probably lymphocytes.

That sensitivity is cellular is shown by the fact that typical tuberculin reactions can be elicited in the avascular cornea and that fibroblasts or macrophages of tuberculin-sensitive animals grown in tissue culture are killed by tuberculin.

5. *Contact allergy*, exemplified by poison ivy, shows the same experimental characteristics as tuberculin-type sensitivity. Since, however, the actual antigen is formed by combination of the allergen (a simple chemical compound) with skin protein, sensitivity can only be elicited by application of allergen to the skin, and the reaction differs in histologic detail from the tuberculin reaction.

Serum disease is not a separate type of hypersensitive process but rather is the name given to the hypersensitive reactions resulting when antigen is still present in the organism, several days after its injection, as sensitivity appears. The reactions may be of one or more of the types mentioned.

All hypersensitive responses obey the following immunologic criteria:

Sensitivity is produced by a sensitizing exposure to antigen followed by a characteristic induction period. The response can only be elicited by specific (that is, the sensitizing) antigen, but is characteristic only of the appropriate type of sensitivity, not of the nature of the antigen.

After sensitivity has disappeared, it re-

appears after an antigen injection (the anamnestic response) more rapidly than it appeared after the original sensitizing injection (the primary response).

Finally, true sensitivity can be passively transferred, with serum or with cells.

Certain nonimmunologic processes can give the same final pictures as the hypersensitive reactions discussed. Thus abnormalities in the physiologic mechanism for histamine release can give anaphylactic or atopic symptoms. Similar (anaphylactoid) phenomena result from injection of such things as peptone or trypsin which cause cellular damage, with histamine and heparin release.

The *Schwartzman* reaction appears to depend in part on the same mechanism as the Arthus but is not produced by antigen and antibody.

The eye has been studied immunologically from a number of standpoints. Antigenic substances have been isolated and, in some instances, characterized in each of the main ocular structures. Of great interest are antigens in the lens and uveal tract which appear to be organ rather than species specific. Large molecules (antigen or antibody) penetrate the blood-aqueous barrier slowly but in considerable amounts in either direction. Thus antigens in the eye can cause general sensitization; and conversely the eye participates in general sensitivity. Antibody is also produced locally in the eye (iris and ciliary body).

Repeated or protracted anaphylaxis produces in the eye only a mild infiltration of polymorphonuclear leukocytes in the optic nervehead. The wheal and flare has never been properly studied in the eye; but an investigation has been carried out on the effects of locally injected histamine. The main finding was edema of the ciliary body, transudation of serum into the anterior and posterior chambers and the vitreous but no cellular exudation, and slight bullous keratitis.

The Arthus reaction, produced in the eye with known amounts of antigen and antibody, gives rise to a violent uveitis with histopathologic changes much like those of the Arthus reaction elsewhere.

The tuberculin reaction gives reactions which depend on the route of injection of tuberculin: a uveitis after anterior chamber or vitreous injection, a typical interstitial keratitis after intracorneal injection, phlyctenules after instillation in the conjunctival sac.

A great number of experimental studies have been carried out on serum disease of the eye—all suffer from the interpretative disadvantages that multiple antigens (such as are present in any foreign serum) were used and that animals were sensitized actively (so that no precise statements are possible regarding the types of sensitivity produced or the types of mechanism operating). The use of such a term as "anaphylactic" iridocyclitis presupposes a mechanism which has not yet been demonstrated, and is therefore to be avoided.

The most significant findings of these studies are as follows:

1. After general sensitization (by intravenous or subcutaneous injection of antigen) injection of antigen into the eye gives a reaction.

2. Intraocular injection of antigen in an unsensitized animal gives a reaction appearing at seven to 13 days.

3. In such an animal, subsequent injection of antigen intravenously gives a recurrence of the eye reaction and may even give a mild reaction in the untreated eye.

4. Sensitization of the eye, as in (2), may be accomplished by intravenous antigen injection and simultaneous trauma to the eye.

5. While the majority of experiments were done with vitreous injection of antigen, comparable results are obtained if the anterior chamber is the test site or, for most of the experiments, the cornea.

The fact that cortisone can suppress these reactions, together with internal evidence from the experiments, suggests that many

of the observed reactions may have been of the tuberculin type. It has been found possible to produce eye disease experimentally by creating sensitivity to antigens present in the eye itself, notably in lens and uvea. The principle of "horror autotoxicus," formulated by Ehrlich, suggests that one cannot develop immunologic reactions to one's own body substances. However, this rule appears not to hold for tissues separated by a physiologic barrier from the circulation, such as the eye and the central nervous system (an experimental disease resulting from autoallergy to nervous tissue antigen has been much studied in recent years).

Sensitization to lens was accomplished with the use of staphylococcus toxin as an adjuvant. In sensitized animals, discission or lens injury gave a disease picture like that of phacoanaphylactic endophthalmitis in man. Sensitization to uvea was brought about by the use of killed tubercle bacilli and mineral oil as adjuvants (the so-called Freund adjuvants). In sensitized animals, a diffuse uveitis appeared that was comparable in many respects to sympathetic ophthalmia.

Discussion. Dr. Frederick H. Verhoeff requested further discussion of the reasons for including interstitial keratitis of syphilis as a hypersensitivity reaction. Dr. Verhoeff pointed out that it usually occurs in a congenital infection in which there have been no manifestations of disease for many years, even up to 30 years, when the patient will suddenly show up with a keratitis in one eye. After this quiets down, he may then later come back with the other eye affected, and from time to time he may have recurrences involving either or both eyes. In some newborn infants, the cornea has been found to be full of spirochetes. In some experimental work in which rabbits have been given experimental syphilis, some of the rabbits have developed interstitial keratitis that was in all ways indistinguishable from human interstitial keratitis from a clinical point of view. In these cases, however, plenty of spirochetes could be found but, in the human eyes, which have been examined at the height of the disease, no spirochetes could be found.

Dr. Verhoeff raised the question as to whether or not the spirochetes are not there all along, but could not be demonstrated because they have possibly been broken up into granules during the preparation of the material. He considered it dubious that interstitial keratitis is a sensitivity reaction.

In reply, Dr. Waksman stated he had only two comments. He agreed with Dr. Verhoeff that the question was far from settled. However, he said that interstitial keratitis, in the few cases where it has been found in noncongenital syphilis, always seems to have occurred in the gummatous type of late syphilis and the gumma is usually considered a very violent type of hypersensitive reaction. In a gumma, spirochetes are very difficult to demonstrate. Individuals exposed to antigens in utero change in capacity to respond to that antigen. For instance, if an antigen is introduced at the proper time, the fetus becomes forever incapable of producing antibody to that antigen. He raised the possibility that this may be the case in congenital syphilis, except that around the age of 30 years, or whenever the patient develops his interstitial keratitis, something happens which suddenly enables him to respond to the antigen. He stated he does not know how this could occur and that it is purely speculation.

Another question was asked from the floor as to why Harada disease and Vogt-Koyanaga syndrome were included as immune reactions. Was there any particular evidence regarding these two conditions? The reply was that only the skin test and certain slight similarities to sympathetic disease justified inclusion of these disease entities with immune reactions. Dr. Waksman added that he was very frank in considering sympathetic disease a sensitivity reaction to uveal tissue.

DR. VERHOEFF said that there were two other things about sympathetic ophthalmia which should be pointed out:

1. That it has a characteristic histology.
2. That it always affects both eyes.

He added that in many other diseases which have certain similarities, the second eye is much more likely to be affected than one would suspect from pure chance. This is particularly true in conditions such as tuberculous uveitis. However, it does not always affect both eyes as one would expect if it were a general sensitivity reaction such as Dr. Waksman had previously described.

DR. WAKSMAN stated in conclusion that a lot has been written on elective "weakness" in the second eye when something has happened to the other. He stated he did not know how to evaluate that, and that he had no experimental grounds on which to base an opinion.

The last question that was asked from the floor was whether lens substance had ever been injected in oil in order to produce hypersensitivity. Dr. Waksman replied, he did not know of any experimental work having been done on that, and he thought it should be done, suggesting possibly mineral oil as a vehicle.

David H. Scott,
Recorder.

NEW YORK SOCIETY FOR CLINICAL OPHTHALMOLOGY

February 7, 1955

DR. FREDERICK H. THEODORE, *president*

CLINICAL ELECTRORETINOGRAPHY

DR. JERRY H. JACOBSON: The electrical potential change developed by the retina upon stimulation by light can be recorded by a technique known as electroretinography. This method, developed primarily by Karpe in Sweden, has been performed in the Department of Electrophysiology of the New York Eye and Ear Infirmary for the past five years.

The technique consists of the use of a modified electrocardiograph or electroencephalograph, and a pickup electrode, consisting of a silver-silver chloride wire which is held in place at the limbus with a contact lens. The method is simple and nonpainful. There have been no harmful effects.

The electroretinogram thus recorded has been found to provide interesting information about several disease processes. In retinitis pigmentosa, the retinogram will provide for early diagnosis, it is believed. In every case of this disease, no matter how early, the retinogram is completely extinguished. It is felt that this early diagnosis is extremely important if any therapy is ever to be of value. It is also felt that this test will provide an objective means of evaluating therapy.

In retinal detachment, there is some indication that the prognosis of an individual case can be judged by the test.

In retinal vascular disease, the amplitude of the b-wave of the graph is proportional to the retinal blood supply. This has been used recently in evaluation of several vasodilator drugs and stellate-ganglion block. There has been no correlation found between severity of glaucoma and the electroretinogram.

By the use of a stroboscopic source of repetitive light stimuli it is possible to determine objective flicker-fusion frequency. When coupled with monochromatic filtered light sources, this sort of stimulus may eventually produce interesting findings relative to cone or macular function.

This would be of great interest, especially in cases of cataract, where the fundus cannot be visualized. At present, using the dark-adapted eye technique now standard, we can get an indication of the total rod function, primarily of the peripheral retina. This has been found valuable but, if the newer techniques will allow for accurate evaluation of macular function, the test will be of

greater significance. A motion picture film describing the basic technique of the test was shown.

Discussion. Dr. Arthur Linksz said that he enjoyed the paper very much, and that the film illustrating the technique of electroretinography was excellent. He asked about the value of electroretinogram in amblyopia ex anopsia. Dr. Jacobson replied that he had had no personal experience with electroretinograms in amblyopia ex anopsia, but that there is a report in the literature which states, he believed, that the retinogram is normal in these cases. This is what would be expected, *a priori*, since the inhibition of vision, if we can call it that, is almost certainly a function of higher centers, not the retina.

Dr. Isadore Givner stated that some of the cases reported in the literature as unilateral retinitis pigmentosa have been questioned. It seemed to him that electroretinograms might be a satisfactory way of differentiating between primary and secondary pigmentary retinal degeneration. He asked whether one could definitely make a diagnosis of retinitis pigmentosa by means of electroretinograms.

Dr. Jacobson answered that they had had one case that was thought clinically to be unilateral retinitis pigmentosa. The patient did, in fact, show an extinguished potential in one eye, and an almost normal one in the other. In regard to the differentiation between primary and secondary pigmentary retinal degeneration, the electroretinogram has been almost normal or better in every case of secondary degeneration examined, with a few exceptions which were definitely subnormal. These cases were never, however, of the extreme low or zero level of primary disease.

Dr. Max Chamlin asked whether Dr. Jacobson had any experience in attempting to determine by electroretinogram whether loss of vision was retinal or cerebral.

Dr. Jacobson replied: In the determination of whether a lesion is in the retina or further on in the nervous chain, the use of combined simultaneous electroretinogram and electroencephalography has been found very useful. The disturbance of the alpha rhythm of the electroencephalogram upon visual stimuli occurs after a definite time interval following the development of the electroretinogram. The use of this combined electrophysiologic measurement, as described by Monniér and François, is a very valuable technique. We are doing some of this work at present.

Dr. Rollett inquired whether Dr. Jacobson had experience in testing optic atrophy.

Dr. Jacobson replied that in optic-nerve atrophy, where there is no intrinsic retinal disease, the lesion is in the third neuron of the chain, beginning with the ganglion cell and progressing toward the brain. In this sort of case, the retinogram is normal, since it originated in the cells of the retina more distal to the central nervous system. This has been our experience.

Surgical treatment of angiomatosis retinae

Dr. Bernard Kronenberg discussed the early history of the recognition of this entity by von Hippel and its relationship to angiomatous cysts of the cerebellum as pointed out by Landau. The disease, Dr. Kronenberg said, progresses to total blindness if not treated in its early stages. The treatments reported were X ray, radium, and diathermy.

Dr. Kronenberg presented a case which he treated with diathermy. He followed the patient for six years and showed color slides of the early changes which took place. The patient did not permit an operation until edema developed in the macula. As a result, the vision retained was not as good as if the patient had been operated in an earlier stage. Dr. Kronenberg therefore stressed the importance of early surgery in these cases.

Discussion. Dr. Max Chamlin asked what happens to these dilated vessels after surgery.

Dr. Kronenberg replied that these vessels

shrink. They become much narrower and almost normal in size. The last three slides show this and the end-result shows that the cyst has been obliterated.

Dr. Theodore asked if there were only 150 cases of angiomatosis reported. Dr. Kronenberg said it sounds unusual, but that there are only approximately 150 cases reported.

Wound healing of iris

Dr. Walter Kornblueth: The clinical observation that the iris does not show any evidence of regeneration of its tissue elements following aseptic iridectomy has never been satisfactorily explained. Up to date there have been very few studies on the healing process of the human iris and only little experimental work on this subject in animals.

To investigate this unusual lack of proliferation of the cells of the iris following injury, tissue culture of the human iris was performed in collaboration with Dr. Tannenbaum of the Cancer Research Institute of the Hebrew University in Jerusalem. The material was obtained from various surgical procedures.

All the different cellular elements of the iris, except for those derived from blood vessels, proliferated in these cultures. The latent period of the outgrowth of cells was very long and the rate of growth slow. Irises taken from cataract cases grew more readily than those obtained from patients suffering from primary narrow-angle glaucoma. Some clinical and very preliminary experimental evidence was presented to show that aqueous humor might actively inhibit cell proliferation in tissue culture. This work will be continued.

Discussion. Dr. Kornzweig raised the question of pigment formation in tissue culture, and suggested that it might be an enzyme which helps to form the pigment, since there is no blood there.

Dr. Kornblueth found this suggestion very good and remarked that if the pigment cells grow very slowly, enough of this enzyme might be transferred to the newly formed cells.

Dr. Gartner said that he does not know of any pathologic studies on the subject in this country. He stated that we have known for a long time that iris wounds do not heal, and thanked Dr. Kornblueth for attempting to explain why.

Dr. Levitt asked whether the lack of vascularity of the iris and the aqueous circulation might not be factors in preventing proliferation of the iris cells.

Dr. Kornblueth replied that the lack of vascularity does not prevent proliferation of cells, as can well be seen in wounds of the cornea.

Dr. Posner pointed out that in glaucoma operations we assume that the integrity of pigment epithelium of the iris is required to keep the fistula open. If the pigment epithelium is damaged, the final result is dubious. If the iris stroma does not proliferate under the influence of aqueous, is there any truth in our clinical point of view that the pigment epithelium of the iris has to be present in the fistula?

Dr. Kornblueth answered that in iridencleisis there is a different set up from an aseptic iridectomy where the corneal wound is closed soon and the iris remains in its place bathed in aqueous. The destruction of the pigment epithelium of the iris in surgery might cause a more intense inflammatory reaction in the surrounding tissues which might lead to proliferation of fibroblasts from the adjacent tissue.

Dr. Kestenbaum asked about the effect of the aqueous on iris healing: whether the aqueous prevents normal proliferation mechanically as a circulating fluid, or has some specific effect.

Dr. Kornblueth thought that it is not only the mechanical factor, but that there might also be present in the aqueous some substance which prevents growth of cells.

Dr. Chamlin remarked that some years back Dr. Bernard Samuels claimed that, in

extracapsular cataract extractions in the absence of any infection, there would be no formation of Elschnig pearls.

Dr. Kornblueth agreed that this finding is valid and in keeping with his observations.

Dr. Virginia Lubkin recollected that Dr. Karl Mayer pointed out that the insertion of a small piece of cartilage into active granulation tissue would suppress growth of capillaries until its removal or absorption. This experiment raises the question of the relationship between the healing process and the presence of chondroitin-sulfuric derivatives similar in cartilage, cornea, and iris.

Dr. Kornblueth replied that if it were true that hyaluronidase was present in the aqueous it could explain the inhibition of cell proliferation, as the hyaluronidase is known to inhibit cell growth in tissue culture. Unfortunately, the presence of hyaluronidase in the aqueous could not be proven. Hyaluronic acid, on the other hand, is known to enhance cell proliferation in tissue culture.

Jesse M. Levitt,
Recording Secretary.

MADRID OPHTHALMOLOGICAL SOCIETY

April 21, 1955

Dr. Marin Amat, *presiding*

Isoniazide in uveitis

Dr. Felipe Muñoz Pato pointed out the scarcity of ophthalmic papers in Spain on this subject in contrast to the numerous publications in internal medicine which followed Professor Soriano's work. Probably it is due to inability to demonstrate the tuberculous etiology of many ocular processes in which the most exhaustive examination of the patient shows only old tuberculous lesions calcified in the lung (pleura lymphatics) clinically "cured." It would seem more than probable that a considerable percentage of uveitis cases are of this nature.

Case reports. A woman, aged 49 years, had suffered since 1952 from redness and pain in the right eye. She was treated for three months and many examinations revealed no tuberculous etiology. During that time, vision of the eye was lost and the pain was so intense that the patient accepted enucleation. I saw the patient for the first time two months later, with similar symptoms in the left eye. It was not possible to prove a tuberculous etiology and vision was reduced to finger perception at half a meter. For two and a half months isoniazide was employed and the patient improved. Vision then was 1/10. Treatment was continued at five mg./kg. body weight without further improvements. Then Gewo 339 was prescribed. This is a combination of the hydrazide of nicotinic acid and PAS introduced in Spain under the name of Dipasic. A dosage of 600 mg. (that is, 10 mg./kg. of body weight) was administered for 20 days then discontinued for 20 days, then continued and discontinued in the same manner for three months. With this treatment the vitreous cleared completely and vision returned to 1/4.

In a second case similar to the first, the patient had only one eye, the other having been lost as a result of trauma. She suffered from uveitis and vision was reduced to finger counting at half a meter. She was given Gewo 339 as in the previous case and discharged, completely cured, two and a half months later.

Numerous cases justify the belief that a tuberculous etiology is relatively frequent in uveitis. It seems right to use a trial treatment in those cases in which the etiology is not well determined. The frequency with which the bacillus becomes resistant to the drug and the possibility of dealing with strains already resistant necessitate administering from the beginning a combination of bacteriostatic drugs. The "interrupted" treatment should be continued for at least six

months, especially in those patients who must undergo intraocular operation.

Discussion. Dr. Mario Estenban: With Isoniazide, one is trying to use bacteriostatic action; therefore, one should expect a favorable effect in lesions with Koch bacilli. However, this is different in ophthalmology. Rarely is a tuberculous lesion produced by the direct action of the bacillus focalized in the eye. Mostly the reactions are toxic, allergic, or parallergic in nature and the bacteria cannot be demonstrated.

In the chronic uveitis—the plastic, insidious uveitis in which neither the clinic nor the laboratory has been able to define the etiology—if we have been able to eliminate syphilis, rheumatism, and other infections, we are accustomed to group the disease as tuberculous; not because of the presence of the bacillus but because, as a result of the reaction in the uveal tract, we see the formation of exudates, the clouding of the media, the formation of synechias that may cause seclusion or pupillary occlusion, the production of secondary glaucoma or degenerative changes. It all occurs, insidiously, slowly, with phases of improvement and aggravation, without observation of a characteristic focus and with a lack of bacilli in the study of the enucleated eyes.

It would seem necessary to differentiate between the tuberculous lesions produced by direct action of the bacillus and those that represent a nonspecific reaction of the uvea. In the first instance, the bacteriostatic agents in general should be used and particularly the Isoniazide. In the second group, where there are no Koch bacilli, the influence of a bactericidal or bacteriostatic drug is doubtful.

Dr. Marin Amat: In those cases of negative biologic reactions, with an insidious uveitis and in which all treatment failed, previous to Isoniazide, metylic antigen (Metigeno) was used with satisfactory results except in one case.

With the appearance of Isoniazide and with the satisfactory outcome of its use in tuberculous processes and especially in tuberculous meningitis in which, at the Hospital Rey, 85 percent of cures were obtained, it has been decided to employ the Isoniazide with streptomycin in those cases of uveitis with suspected tuberculous etiology—Isoniazide orally (5.0 mg./kg., daily); streptomycin (2.0 gr. per week) in intramuscular injections and as long as necessary. The combined drugs are also satisfactory for treating recurrent hemorrhages in the vitreous in young people.

Referring to Dr. Muñoz Pato's comment that Isoniazide is a drug which favors hemorrhage, I might say that, in 100 cases studied, we have, in only one case, seen capillary hemorrhages around both optic discs, arranged in a crown fashion and not more than two mm. in length. The case was that of a woman who required a high dosage (800 mg.) As soon as the dosage was decreased, the hemorrhages disappeared.

Dr. Aguilar Muñoz: I agree with Dr. Muñoz Pato about the beneficial use of this product for the treatment of ocular tuberculosis. I would like to cite a case with a choroidal tubercle, which I followed for two years. It was treated solely with Isoniazide. Complete cicatrization and pigmentation were obtained in about eight months. No relapses occurred.

Diamox in ocular hypertension

Dr. Aguilar Muñoz, Dr. Del Rio Cabañas, and Mr. Calvo Picó said that Diamox is a sulfonamide derivative that has a definite application in ocular hypertension. In most of the cases it has an energic hypotensive action. At the present moment, it is used to produce a tension level which will permit surgery.

Of the nine cases treated, intolerance symptoms were found only in a girl, aged four years, with buphthalmia. The cause may have been the excessive dosage which was used (375 mg. daily). The symptoms of intolerance disappeared rapidly as soon as Diamox was withdrawn. In all cases, the

tension dropped a few hours after the beginning treatment.

Discussion. Dr. Garcia Alix: We believe it is not sound to discontinue the use of miotics when employing Diamox in acute glaucoma, since both medicaments have a synergic action. We should use all means available to lower the tension in all these cases.

Dr. Galindez Iglesias: In none of my cases were somnolence or gastrointestinal symptoms present but, as was reported here tonight, I have found acroparesthesia, at times early and of marked intensity.

At the beginning I used to administer 750 mg. the first day and 500 mg. daily thereafter. In some cases, I used only 250 mg. per day. I would like to mention a few examples:

The first case was that of a glaucoma secondary to a penetrating corneal transplant (8.5 mm in size). Tension fell from 55 to 30 mm. Hg. I had to perform a perforating cyclodiathermy.

The second case was a narrow-angle glaucoma with cataract. Diamox was administered to control the tension prior to a first antiglaucomatous operation.

Based on the diminution of aqueous secretion which this drug produced I have used it in the following cases: (1) A perforated corneal ulcer. Diamox reformed the anterior chamber. (2) A cataract was extracted intracapsularly by phakoerisis. Ten days later a few sutures were loose, a small hemorrhage was present, and the anterior chamber was absent. With Diamox the chamber rapidly reformed. (3) A cataract operated elsewhere, without anterior chamber, with hypotony, and pain. With Diamox the anterior chamber was almost completely reformed.

Dr. Aguilar Muñoz thanked Dr. Bartolozzi and Dr. Garcia Alix for their discussions. The results with Diamox have been splendid. In cases of absolute glaucoma, it has conditioned the eye for uneventful surgery. The pathogenesis of glaucoma is not clear as yet. Some theories are valid as, for example, that of Kleinert which admits a sclerosis of the limboscleral vessels at the area of the aqueous veins of Ascher. These vascular changes would produce an edema of the region and thus would provoke the closure of the vessels—the closure of the aqueous veins augmenting the resistance for aqueous outflow. This theory would agree well with the role of Diamox. As a strong diuretic it would cause the disappearance of limbal edema and congestion of blood and aqueous vessels, relieving the circulation of both, as well as the ocular hypertension.

Olga Ferrer,
Translator.

Ophthalmic Miniature

The eye should rest, in reading, upon the bottom of the socket which contains it, and that position of a book which favors that easy state of the eye will seldom give it any pain or injure vision.

Benj. Rush: Letter to James Rush,
May 31, 1804.

AMERICAN JOURNAL OF OPHTHALMOLOGY

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SPRING MEETINGS, 1956

The 92nd annual meeting of the American Ophthalmological Society, Alan C. Woods presiding, was held at the Homestead, Hot Springs, Virginia, May 31, June 1 and 2, 1956. One hundred and nineteen members and 28 guests attended. Twenty-one papers, for the most part of clinical interest, were read and the discussions of each were lively and interesting, sparked as they were by our senior and most loved member, F. H. Verhoeff. The hot weather was shattered by a prolonged and cooling rain which came on the last day of the meeting, holding off just long enough to permit completion of the golf and skeet tournaments which are always of considerable local interest and selective importance.

Frederick C. Cordes of San Francisco, California, was elected president and Walter

S. Atkinson of Watertown, New York, vice-president for 1957. The Howe Medal of the society was awarded to Bernard Samuels of New York City for his many contributions to ophthalmology. The next meeting of the society will be held at the Homestead, May 30, 31, and June 1, 1957.

The Section on Ophthalmology, A.M.A., and the Association for Research in Ophthalmology met concurrently from June 11th to June 14th in Chicago. Unfortunately, the weather decided to break all heat records for early summer and, in spite of air conditioning here and there, became nearly intolerable. This and other factors had considerable effect on the attendance at both meetings, which is most discouraging to the officers responsible for the difficult job of getting together excellent programs. Even many of the members who live in the Chicago area were absent, which is unfortunate for they missed many fine papers and exhibits.

The Section presented 18 papers that were ably discussed. It is always difficult to pick out the most outstanding contributions in any of our meetings, for what may appeal to one does not always do so to another, especially with a program so well rounded as this one was.

A. D. Ruedemann, Sr., in his chairman's address, discussed foveal co-ordination as a major factor in visual training. Francis C. Grant, neurosurgeon of Philadelphia, was the guest-of-honor of the Section. The title of his address, co-authored by T. H. Hedges of Philadelphia, was "Ocular findings associated with meningiomas of the tuberculum sellae." He pointed out that, among other important ocular signs, the careful recording and study of the visual fields were the most important from a diagnostic but particularly from a prognostic viewpoint.

The session was made particularly noteworthy by the appearance on the program of the chairman's son, A. D. Ruedemann, Jr., of Detroit, who gave a good paper on vertical muscle imbalance and scoliosis. W. E. Krewson, 3rd, in his discussion, pointed out to the members that this was the only time, so far as could be determined, that such an event had occurred in a Section meeting, and how heart-warming it must be to the chairman to have such a son to follow in his steps.

Since the papers will shortly be published in the *A.M.A. Archives of Ophthalmology*, it is not necessary here to give abstracts or further details regarding them. Their publication will be looked forward to with much interest, particularly by those who attended the meeting, for obviously the authors could only cover the highlights in their presentations due to the time limits.

A special business meeting was held on the evening of June 12th. Reports of various committees had been printed and distributed prior to the meeting so, presumably, each member had the opportunity of reading them ahead of time. This is a good idea and a great time saver. Two new and important joint committees were approved and appointments made. These are (1) The Committee on Research in Eye Disease, which will be the subject of an editorial in THE JOURNAL in a future number, and (2) The Committee on Eye-Banks, whose purpose will be to bring order and integrity in a field of ophthalmic activity that has been found by a careful preliminary study to be in serious need of these qualities.

Ralph O. Rychener, chairman of the Public Relations Committee, gave his report, the details of which will be found in the printed *Transactions*. The difficulties encountered by his committee were outlined and a good discussion on measures to alleviate them was entered into. The solutions of many of the problems are not, at the moment, immediately apparent but progress is being made and the committee obviously has the wholehearted support of the members of the Section.

The business meeting concluded with a talk by Ralph H. Pino of Detroit, on the subject of "Distribution responsibilities of the specialities represented in the Scientific Assembly," in which he advocated the devel-

opment of university training centers for office assistants.

The officers of the Section elected for 1957 are Algernon B. Reese of New York City, chairman; Hedwig S. Kuhn of Hammond, Indiana, vice chairman; and Harold G. Scheie of Philadelphia, secretary. Ralph O. Rychener of Memphis, Tennessee, was elected delegate of the Section to the House of Delegates, A.M.A., and Harvey E. Thorpe of Pittsburgh, alternate delegate.

The $250.00 prize for the best scientific exhibit from the Section was awarded to Bertha A. Klien, of Chicago, for her outstanding exhibit on "Survey of pathogenesis and treatment of retinal venous occlusions." This exhibit was also awarded a Certificate of Merit by the A.M.A. Honorable mention was awarded to David Volk of Cleveland for his fine exhibit of "Aids to subnormal vision." There was a total of nine exhibits representing the Section, all of which were first class indeed.

The Gold Medal of the Section for service to ophthalmology was awarded to Derrick Vail of Chicago, who was deeply moved by this manifestation of approval by his colleagues.

At the meetings of the Association for Research in Ophthalmology, under the skillful chairmanship of William B. Clark of New Orleans, 39 papers of high quality in the field of experimental ophthalmology were read and discussed. A surprising number were of clinical interest and application so that even the middle-aged clinical ophthalmologists came away with a number of new and useful ideas, as well as being deeply impressed with the skill and precision of the work of his laboratory brethren. It is exciting indeed to see the development and vigorous growth of this organization, now totalling almost a thousand members. Its influence on scientific medicine is impressive and the work of its members is elevating and broadening the field of our science to a remarkable degree in a relatively short span.

The following were elected officers of the Association for Research for the ensuing year: Theodore E. Sanders of St. Louis, chairman; Lorand V. Johnson of Cleveland, secretary-treasurer; and Harold F. Falls of Ann Arbor, Michigan, the new trustee. Arthur J. Bedell of Albany, New York, F. Phinizy Calhoun, Sr., of Atlanta, Georgia, Frederick C. Cordes of San Francisco, Robert J. Master of Indianapolis, and Derrick Vail of Chicago, were elected honorary members.

At the official banquet of the association, W. Morton Grant of Boston was awarded the Proctor Medal of the association for his scientific achievements in the field of ophthalmology, notably glaucoma. Dr. Grant accepted the medal with a modest and charming speech in which he affectionately lauded three ophthalmologists who had great influence on his career. These are Paul Chandler, David Cogan, and Frederick H. Verhoeff.

The next meeting of the Section and the Association for Research will be held in New York City, June 2 to 6, 1957.

Derrick Vail.

WILMER MEETING

The 15th clinical meeting of the Wilmer Residents Association was held at the Wilmer Ophthalmological Institute in Baltimore on April 19, 20, and 21, 1956. Almost 400 former members of the Wilmer house staff and guests registered during the three days of the meeting.

The first two days of the meeting consisted of a total of 29 papers covering a wide range of subjects. As has been the usual tradition, each of the papers was discussed very ably by Dr. Frederick Verhoeff and others.

The opening paper, "Ocular manifestations of herpes simplex," was presented by the new Professor of Ophthalmology and Ophthalmologist-in-Chief, A. Edward Maumenee. In his presentation Dr. Maumenee discussed the clinical manifestations of herpes simplex and outlined the current experimental work being carried out at the

Wilmer Institute with this virus. The second paper was "Surgical treatment of thyrotropic exophthalmos" by W. Jerome Knauer, Jr., present senior resident. Dr. Knauer included in his presentation a movie showing the technique of lateral orbital decompression. Perhaps the most exciting paper of the entire meeting was "The use of ultrasonics in ocular diagnosis" by William F. Hughes, Jr., and G. Henry Mundt, Jr. The authors discussed their technique of use of this new device and presented their experiences with it in cases with intraocular tumors, intraocular foreign bodies, and retinal detachment. Two papers on toxoplasmosis completed the morning: the first, "Studies on Toxoplasma," by Jack S. Gans, and the second, "Further studies on the role of toxoplasmosis in the etiology of endogenous uveitis," by Alan C. Woods. Dr. Woods' paper comprised the cases of endogenous uveitis seen at the Wilmer Institute between 1953 and 1955 and compared this series with previously reported series.

The absence of Dr. Jonas Friedenwald from this year's meeting was deeply felt by everyone, and Dr. Alan C. Woods paid tribute to his many accomplishments.

In the afternoon there were three papers by members of the present Wilmer house staff. J. Lawton Smith presented ocular manifestations in a series of 465 cases of rheumatoid arthritis. Shepard N. Dunn presented the long-term follow-up of a series of 38 cases of primary tumors of the iris. John F. Hannon presented a most interesting paper on a series of vitreous hemorrhages associated with sickle cell-hemoglobin C disease. James Duke and Howard Naquin presented the clinical and pathologic findings of the ocular manifestations of a rather rare syndrome, lethal midline granuloma. Robert Schimek presented a preliminary report on hypophysectomy for diabetic retinopathy and reported three cases in which this had been carried out, the longest with a follow-up of nine months. In the discussion of this paper Frank Walsh presented an additional case. Two papers on visual aids for the partially blind were presented, one by Richard E. Hoover and another by Louise Sloan and Adelaide Habel. The last paper of the afternoon was "A laboratory and clinical study on a new antibiotic," by Ronald M. Wood, W. J. Knauer, Jr., and Margaret Sherwood. They presented their experiences with the new antibiotic, Capromycin.

The first three papers on Friday morning were on glaucoma. Howard Stone presented "Recent studies in tonography"; Malcolm Bick presented "Pigmentary glaucoma in the female"; and David A. Rosen presented "The effect of a ganglionic blocking drug, pentapyrolidinium, on intraocular fluid dynamics." Benjamin Rones and Lorenz Zimmerman discussed diffuse malignant melanoma of the iris and presented clinical and pathologic material. Angus MacLean presented three cases of Thorazine toxic amblyopia and, in the discussion of his paper, a number of other cases were described by other ophthalmologists. Cornelius E. McCole, George Magee, and Mary Argue presented the use of DFP in esotropia and described the experience with this drug in the orthoptic clinic of the Wilmer Institute. Carl Kupfer, a member of the house staff on leave to the Air Force, discussed the treatment of amblyopia ex anopsia in adults and reported on seven cases. The last paper of the morning was "Possible sources of postoperative infection in eye hospitals," by Ronald M. Wood, M. J. Grieves, and Laurence Senterfit. One of the sources of infection was found to be in the soap used in the scrub by doctors and nurses. This soap was found to be heavily contaminated and the authors stressed the importance of insuring sterility of this soap.

The first two papers on Friday afternoon were "Adenoma of Harder's gland in mice," by Walter H. Benedict and the "Effect of local anesthetics on regeneration of corneal epithelium," by William G. Marr, Laurence Senterfit, and Ronald M. Wood. In this latter paper the authors continued work which

had been reported at previous meetings. Arnall Patz discussed the factors influencing oxygen-induced retrolental fibroplasia and discussed particularly the rapid versus the prolonged oxygen withdrawal. He showed in his experiments that rapid withdrawal from oxygen is better than prolonged withdrawal. Herman Goldberg reviewed the cases of pseudotumor of the orbit that have been seen at the Wilmer Institute. There were two papers on retinal detachment surgery, one by John M. McLean on some problems of retinal detachment surgery, and the second on scleral resection for retinal detachment by L. Harrell Pierce. Dr. Pierce discussed the method of scleral resection being carried out at the Wilmer Institute at the present time and illustrated his discussion with a motion picture. The last two papers of the afternoon were "Recent biochemical studies on diabetic retinopathy," by Burton M. Pogell and "Current studies on intraretinal recording of nerve impulses and electroretinogram in the unopened cat eye," by Kenneth T. Brown and Torsten Wiesel.

On Friday evening approximately 200 members and guests assembled at one of the local hotels for an informal dinner and dance. The present members of the Wilmer house staff literally sang for their suppers with their annual skit.

On Saturday morning joint medical and ophthalmologic rounds were held in Hurd Hall by A. McGehee Harvey and A. Edward Maumenee. The meeting was brought to a close by the now traditional Neuro-Ophthalmologic Clinic by Frank B. Walsh. As usual, this clinic presented an exciting and exotic collection of neuro-ophthalmologic cases.

At the end of the meeting it was announced that the 16th annual Wilmer Residents Meeting would be held in Baltimore on April 4, 5, and 6, 1957.

Howard Naquin.

OBITUARY

ALAN SEYMOUR PHILPS, F.R.C.S. (1906-1956)

Many American ophthalmologists knew Seymour Philps either personally or through his writings, particularly his excellent and useful book *Ophthalmic Operations*. We liked him very much indeed. We liked his friendliness and cheerfulness, his integrity, his keen mind, and the lightning flash of his wit and intelligence. We were saddened to hear of his serious illness, beginning two years ago, which he bore with inspiring fortitude, and we are depressed to learn of his death on April 26, 1956, at the early age of 50 years. We shall miss him.

Philps was educated at Aldenham School and took his medical work at St. Bartholomew's Hospital, London, qualifying in 1929. He became a fellow of the Royal College of Surgeons in 1931. He held several house appointments at the Royal Westminster Eye Hospital and, in 1932, became the out-patient officer at Moorfields. In 1934, he became chief assistant in the eye department at Barts, and, in 1940, a full surgeon at Moorfields. He was an ophthalmic specialist in the R.A.M.A. during the last war and took a very active part in the Normandy landings.

In 1948, he became surgeon in charge of the eye department at Barts and, a year later, advisor in ophthalmology to the Ministry of Transport. His book *Ophthalmic Operations*, appeared in 1950. It is beautifully illustrated with his own drawings and photographs. He is chiefly known in this country for his surgical skill and for his work on scleral resection and keratoplasty. He devised a number of ingenious devices to make eye surgery more efficient and safe. We owe him a debt of gratitude and remembrance.

Derrick Vail.

CORRESPONDENCE

Prof. Ishihara's birthday

Editor,
American Journal of Ophthalmology:

The 77th birthday party of Prof. Shinobu Ishihara was held by his pupils in Atami City, which is near Tokyo, on November 5, 1955. At the party on that day, he talked with us and told of his color-blindness testing work for 40 years and discussed how to use his test. Professor Ishihara, among other things, mentioned that it had come to his notice that his charts are now being used for testing the degree of any kind of color blindness. This is not his aim. The chief purpose of Ishihara's charts is for finding accurately and quickly whether or not a person is color blind. He emphasized that his charts for the classification of color deficiency are not complete but that it is better to have something to go on than nothing at all.

(Signed) Tutomu Sato,
Bunkyoku, Tokyo, Japan.

Ophthalmologists for Africa

Editor,
American Journal of Ophthalmology:

We are making a national survey at this time to locate ophthalmologists, or physicians desiring to train in ophthalmology, who might be interested in serving in Africa with Eyes for Africa, Inc., a nonprofit, Christian corporation dedicated to treating Africans with eye disease, of which there are hundreds of thousands.

We are hoping that The Journal might know of someone who would consider volunteering his services for such work. We would greatly appreciate any assistance.

(Signed) Burton Lindau,
1700 Canal Street,
Room 372,
New Orleans, Louisiana.

BOOK REVIEWS

Medical Research: A Midcentury Survey. Published for The American Foundation, Westbrook, Connecticut. Boston, Massachusetts, Little, Brown and Company, 1955. Two volumes: I. American Medical Research: In Principle and Practice (765 pages); II. Unsolved Clinical Problems: In Biological Perspective (740 pages). Price: (2 vol.) $15.00.

My attention to these fascinating volumes, so fraught with meaning to all our people and to medical scientists in every field, was directed by the able editor of the *A.M.A. Archives of Ophthalmology*. I am grateful to him for this courtesy and I am eager to pass on to all of our subscribers the information that these volumes exist and to urge them to read them carefully. An editorial, or leader as it is called, in the *Lancet* of January 7, 1956, suggests that these studies "may have as much influence on American medical research as (the famous) Flexner's reports of 40 years ago had on American medical education."

The work is a massive one, completed after 15 years of study, under the leadership and authorship of Miss Esther Everett Lape, member-in-charge of the American Foundation Studies in Government, her immediate associates, and a committee of consultants whose names are by-words in medical education and research.

The first volume is concerned with (1) medical research in the perspective of biological, chemical, physical, and mathematical sciences and discusses the orienting of medical research under the umbrella of these disciplines; (2) current trends and problems in the United States, incorporating concepts, conditions, trends, role of government and its relation with science, and social influences; (3) research agencies, describing current and specific university departments, medical schools, foundations, research institutes, industrial organizations, governments, societies, and so forth; (4) clearing results and controlling products of medical research. This chapter includes ways and means, such

as the scientific literature, government controls of commercial products, standardizing influence of professional groups, and influence of patents.

The second volume deals with unsolved specific clinical problems in the biological perspective, which are chiefly metabolic concepts, cancer, infertility, arteriosclerosis, hypertension, connective tissue, tuberculosis, virus diseases, alcoholism, and the biology of schizophrenia.

The main thesis for these two volumes is the significance of basic research for medical progress. Most of us are aware of the importance of basic research, particularly as it pertains to our own many unsolved problems in ophthalmology, and more and more of us are becoming convinced of the need to tell the people of this need. Our task is greatly lightened by the information contained in this stupendous work.

You will find, scattered here and there in each of these volumes, references to important research investigations by ophthalmologists and eye research centers, such as in retrolental fibroplasia, the congenital cataract due to virus (rubella) in pregnancy, the physiology of the eye, the evolution of vision in the embryo, and the application of basic research to the solution of clinical problems of ophthalmology.

Full justice to this work cannot possibly be given in a short book review. It is too important. Our purpose is to publish an editorial later that will discuss in more detail the many provocative thoughts engendered by these studies. It is a pleasure to join in the swelling chorus of acclaim that is rising throughout the English-speaking medical world accorded to these volumes. All of us interested in medical research—and few of us aren't—should get these volumes and study them in the quiet of our libraries for the inspiration and important information they contain. We shall be the better for it.

Derrick Vail.

Optics of Contact Lenses. By A. G. Bennett. London, Association of Dispensing Opticians, edition 2, 1956. Paperbound, 81 pages, 56 figures. Price: $1.80 postpaid.

Herschel, in 1845, first suggested the idea of contact lenses and considered them the most direct means of treating astigmatism. The postwar period has witnessed many improvements and a marked expansion in their use. When astigmatism is corrected with spectacles, the retinal image is distorted, owing to differing magnifications in the two principal meridians. With contact glasses the intervening fluid can neutralize but 9/10 (336/376) of irregularities which affect only the front surface of the cornea. Even if the contact lens is correctly centered, a prismatic effect may be created by the sag of the lens upon the eye—base-down for positive power. Compared with orthodox spectacles, contact lenses for distance correction impose a greater accommodative effort on myopes, and a smaller effort on hypermetropes when used in near vision. The manufacture of good contact lenses demands extreme precision, the tolerance of the optic radius being only 0.001 inch, yet plastic material, owing to its springiness, is more difficult than glass to work optically. This compact brochure presents the optical problems of contact glasses most adequately.

James E. Lebensohn.

Medical Progress: 1956. Edited by Morris Fishbein, M.D. New York, McGraw-Hill Book Company, 1956. Clothbound, 373 pages, and index. Price: $5.50.

A short section in this annual publication relating to current medical advances is devoted to ophthalmology. Dr. Manuel L. Stillerman, who has again edited the chapter on ophthalmologic progress, has shown excellent choice and sound editorial judgment. He discusses the present status of toxoplasmosis as a possible cause of uveitis and outlines the treatment. There is a brief discussion of acetazoleamide (Diamox), streptokinase and streptodornase, and hyaluronidase. Recent developments in retinal detachment surgery, especially the scleral buckling operation advocated by Schepens, are described.

William A. Mann.

ABSTRACT DEPARTMENT

EDITED BY DR. F. HERBERT HAESSLER

Abstracts are classified under the divisions listed below. It must be remembered that any given paper may belong to several divisions of ophthalmology, although here it is mentioned only in one. Not all of the headings will necessarily be found in any one issue of the Journal.

CLASSIFICATION

1. Anatomy, embryology, and comparative ophthalmology
2. General pathology, bacteriology, immunology
3. Vegetative physiology, biochemistry, pharmacology, toxicology
4. Physiologic optics, refraction, color vision
5. Diagnosis and therapy
6. Ocular motility
7. Conjunctiva, cornea, sclera
8. Uvea, sympathetic disease, aqueous
9. Glaucoma and ocular tension
10. Crystalline lens
11. Retina and vitreous
12. Optic nerve and chiasm
13. Neuro-ophthalmology
14. Eyeball, orbit, sinuses
15. Eyelids, lacrimal apparatus
16. Tumors
17. Injuries
18. Systemic disease and parasites
19. Congenital deformities, heredity
20. Hygiene, sociology, education, and history

1

ANATOMY, EMBRYOLOGY, AND COMPARATIVE OPHTHALMOLOGY

Burian, H. M., Braley, A. E. and Allen, L. **A new concept of the development of the angle of the anterior chamber of the human eye.** A.M.A. Arch. Ophth. **55**:439-442, March, 1956.

Evidence is presented which is not in harmony with the previously accepted theory that a measureable amount of tissue must atrophy and be resorbed between the tissues of the trabeculum and the iris-ciliary body. On the new basis, mesodermal remnants do not exist. Instead, it is shown that persistent adherence of the iris root to the trabecular tissue can give the gonioscopic appearance formerly attributed to embryonic mesodermal remnants. (4 figures)

G. S. Tyner.

Calamandrei, G. and Camici, A. **Structure of Bruch's membrane.** Gior. ital. oftal. **8**:527-536, Nov.-Dec., 1955.

An interesting study was made on Bruch's membrane from eyes excised for various reasons. The membrane is formed of two parts, an outer elastic portion, continuous and probably forming part of the subcapillary layer of the choroid, and an inner portion, separating the choroid from the retina, between the posterior pole and the ora serrata. At this site the elastic layer is subdivided into various sheets. (4 figures, 10 references) V. Tabone.

Cooper, S., Daniel, P. M. and Whitteridge, D. **Muscle spindles and other sensory endings in the extrinsic eye muscles; the physiology and anatomy of these receptors and their connections with the brain.** Brain. **78**:564-583, 1955.

It is suggested that the presence of muscle spindles may have been denied because they were sought in transverse sections of the muscle belly, instead of the more proximal portion of the muscle, where they are actually located. There are about fifty muscle spindles in each extrinsic eye muscle, about as many as in a lumbrical muscle of the hand. This histologic finding was confirmed with electrophysiologic studies. Further work indicated that some of these receptors have their cells of origin in the mesencephalic nucleus of the fifth nerve. Thus, every eye movement is perceived in the brain stem. The collateral comparative anatomy is considered in some detail. (30 figures, 51 references) Harry Horwich.

François, J. and Neetens, A. **Vascularization of the optic pathway.** Brit. J. Ophth. **40**:45-52, Jan., 1956.

This is the third in a series of studies dealing with the architecture of the vascular system of the optic pathway. The entire optic nerve system of a patient who had died of congestive heart failure is dissected out soon after death and preserved in a fixing solution, then frozen, sectioned and stained. The central artery of the retina is present but although it courses within the optic nerve it does not nourish the nerve itself but rather branches out beyond the lamina cribrosa to serve only the retina. Collateral branches of the artery also exist but they too are destined for the retina. Back of the chiasm, the axial vascular system is replaced by several small independent arterioles. The arterial branches run anteroposteriorly while the venous branches run radially. The vascular arrangement in the intracranial temporal part of the optic system indicates a rarefaction of capillary blood supply which may be significant in vascular disease, intracranial tumors and infectious diseases. (9 figures, 6 references)

Morris Kaplan.

Miyata, N. **Aqueous vein in normal man.** Acta Soc. Ophth. Japan **60**:188-198, April, 1956.

Ascher's glass-rod phenomenon, Kleinert's compensation maximum, and clinical and neoprene cast findings of the aqueous vein in nonglaucomatous individuals were compared. Miyata classified the aqueous veins in two categories: 1. thick and isolated and 2. fine and reticular. In the former, the aqueous influx is apt to occur in Ascher's glass-rod test, and the compensation maximum is higher than 101 gm. as a rule. In the latter, the blood influx is apt to occur and the compensation maximum is lower than 100 gm. The findings of the neoprene cast are illustrated by text figures. (4 figures, 2 tables, 31 references) Yukihiko Mitsui.

Pau, H. **Polarization in cornea and sclera.** Arch. f. Ophth. **156**:415-426, 1955.

Polarization and the white color of the sclera are both an expression of molecular structural order in the fibers. (7 figures, 6 references) F. H. Haessler.

Pau, H. **The appearance of cornea and sclera under the polarization microscope.** Ophthalmologica **130**:340-343, Nov., 1955.

Systematic study of the ocular tissues by means of the polarization microscope revealed double refraction to be an optical characteristic of the sclera, the striated muscles, their tendons, the optic nerve sheaths and septa and, to a lesser extent, the parenchyma of the cornea. The phenomenon of double refraction by the tissue elements of the sclera was studied under various experimental conditions, such as drying, inflammation and excessive pressure. (7 figures, 3 references)

Peter C. Kronfeld.

Sverdlick, Jose. **A study of the fixed cells of the corneal stroma by means of Hortega's panoptic method.** Arch. oftal. Buenos Aires **30**:427-430, Nov., 1955.

Ammoniacal silver carbonate staining for microglia may be used with advantage whenever an optimum rendering of minute morphological detail of the corneal connective corpuscles is needed. A series of frontal sections of the corneas of man, horse and rabbit were made; in them, a number of otherwise scarcely visible features became plainly apparent, owing to the different staining properties of the structures concerned. (10 figures, 2 references) A. Urrets-Zavalia, Jr.

2

GENERAL PATHOLOGY, BACTERIOLOGY, IMMUNOLOGY

Cherednichenko, V. **The influence of a proteolitic ferment of the trypsin type,**

Necrosine, on the tissues of the eye in the experiment. Vestnik oftal. **34**:28-30, Sept.-Oct., 1955.

The morphologic and experimental studies at the Kharkov Medical Institute confirm the possibility of the development of traumatic iridocyclitis without the participation of microbes. The author used Necrosine for his experiments, a powerful proteolitic ferment of the trypsin type, which is identical with Metchnikoff's macrophage. This substance was introduced into the cornea of eight rabbits, and in three concentrations into the anterior chamber and the vitreous of 12 rabbits. In a third series, crystallized trypsin was used on 20 rabbits. The eyes were enucleated and examined histologically.

The experiments showed that it caused local necrosis of the cornea and that its introduction into the chambers of the eye caused destructive changes with severe exudative and hemorrhagic inflammation

Olga Sitchevska.

Denig, Rudolf. **Migration of foreign bodies in the anterior chamber of rabbits.** Klin. Monatsbl. f. Augenh. **128**:204-206, 1956.

This is a postscript to the author's paper on the same subject read before the German Ophthalmological Society in 1896. Brass introduced into the anterior chamber of rabbits will under certain conditions migrate. It is assumed that this is caused by the current in the aqueous and it will only occur when the foreign body is surrounded by a layer of leukocytes.

Frederick C. Blodi.

Hallett, J. W., Leopold, I. H. and Inwald, S. **Streptococcal antihyaluronidase in uveitis and primary glaucoma.** A.M.A. Arch. Ophth. **55**:313-319, March, 1956.

The antihyaluronidase and antistreptolysin titers in 63 cases of uveitis from Wills Eye Hospital have previously been reported. In this study the blood serum levels of streptococcal antihyaluronidase were measured by the turbidimetric method in 326 normal persons, 97 patients with uveitis and 40 patients with chronic simple glaucoma. No increase over that of the normal controls was found in any group. Apparently at present the method is only a research procedure and not a routine clinical laboratory test. (4 tables, 15 references) G. S. Tyner.

Michaelson, I. C. **Unilateral budding in new vessel formation in the eye.** Brit. J. Ophth. **40**:36-39, Jan., 1956.

Frequently new vessel formation occurs only on one side of the parent vessel while the other side remains free of budding. It is assumed that there is a factor exciting this neovascularization on the side of the vessel which develops these new offshoots and aqueous fluid seems to have an inhibiting influence on new vessel growth. (6 figures, 2 references) Morris Kaplan.

Straub, W. **Experimental infection with toxoplasma gondii.** Ophthalmologica **130**: 200-208, Sept., 1955.

In previous reports the author described the directions in which toxoplasma spreads after experimental inoculation under the conjunctiva or into the anterior chamber. The study under review concerns itself with the early effects of intracorneal inoculation of rabbits with toxoplasma gondii. The response of the cornea was, on the whole, very slight. In small amounts the protozoon caused practically no keratitis but could be seen to migrate into the surrounding sclera and to spread from there into the uvea as well as into and through the conjunctiva. Vascularity of the host tissue seemed to be essential for growth and multiplication of the protozoon. (7 figures, 1 table, 9 references)

Peter C. Kronfeld.

3

VEGETATIVE PHYSIOLOGY, BIOCHEMISTRY, PHARMACOLOGY, TOXICOLOGY

Becker, B. and Constant, M. A. **The**

facility of aqueous outflow. A.M.A. Arch. Ophth. **55**:305-312, March, 1956.

The perfusion methods of Bárány and Grant provide a direct experimental approach to the measurement of aqueous outflow in the enucleated eye. Fortunately, tonography can be applied to rabbit eyes permitting in vitro and in vivo methods.

The authors report their findings by tonography and perfusion by both methods, and the values obtained by all three procedures are in agreement.

Average values for normal rabbit eyes are an intraocular pressure of 19 mm. Hg, a facility of outflow of 0.35, and a rate of secretion of aqueous of approximately 3.5 cu. mm./min. (5 figures, 3 tables, 15 references) G. S. Tyner.

Centanni, Leonardo. **The effect on the retina of lactic and pyruvic acids in the presence of cortisone.** Rassegna ital. d'ottal. **24**:371-380, Sept.-Oct., 1955.

The author briefly reviews the concepts which preceded his personal research upon enzymatic metabolic activity of the retina. He studied 1. the behavior of lactic and pyruvic dehydrase upon the retina and, 2. the changes in enzymatic activity induced by cortisone. (15 references) Eugene M. Blake.

Centanni, Leonardo. **Succynil-dihydrogenase-oxidase activity of the retina.** Gior. ital. oftal. **8**:482-489, Nov.-Dec., 1955.

With the manometric method of Warburg it was found that 1. the rabbit's retina showed a marked succynil-dihydrogenase-oxidase activity and 2. the high respiratory quotient of this activity was depressed by cortisone. The author observed that similar results were obtained both by the biochemical and manometric methods. (62 references) V. Tabone.

Dardenne, U. and Breuter, H. **The occurrence of steroid hormones in the vitreous.** Arch. f. Ophth. **156**:283-292, 1955.

800 grams of vitreous from the eyes of cattle was analyzed by various methods. In the neutral ketone fraction the presence of approximately 0.1 mg. percent 17-ketosteroid was demonstrable, and in the phenolic fraction 1 γ percent oestron was revealed by paper chromatography. In the neutral nonketone fraction paper chromatography based on the color reaction with antimony trichlorid-nitrobenzol made probable the assumption that an α-alcoholic steroid is present and in the β fraction 0.02 mg. percent cholesterol was found. (3 figures, 39 references) F. H. Haessler.

Fornaro, L. and Lepri, G. **Cortisone and ocular tuberculosis.** Gior. ital. oftal. **8**:510-515, Nov.-Dec., 1955.

Rabbits were first sensitized and then infected through the anterior chamber to produce ocular lesions not unlike those encountered in man under ordinary conditions. Cortisone given subconjunctivally when the inflammation was fully active did not modify the course of the infection and had no effect on the antibiotic therapy which was given concurrently. (6 references) V. Tabone.

François, J., Rabaey, M. and Denucé, J. M. **Paper chromatography studies of the amino acids of alpha-crystallin.** Ann. d'ocul. **189**:103-119, Jan., 1956.

The authors have found 17 amino acids in pure crystallin of ox and man. Most plentiful are the basic amino acids. The composition of α crystallin in the cortex does not differ from that in the nucleus, nor is there any difference between man and ox. Comparing α and β crystallin, the former has a lower concentration of cystine and tyrosine, but a higher concentration of theonine. (12 figures, 2 tables, 22 references) John C. Locke.

Hambresin, L. **Diseases due to eye drops.** Ann. d'ocul. **189**:92-102, Jan., 1956.

The author reviews the local and gen-

eral complications which may result from the topical use of mydriatics and local anesthetics in the eye. John C. Locke.

Ikeda, I., Komi, T. and Morikawa, H. **Nonspecific ocular reactions and adrenocortical lipids.** Acta Soc. Ophth. Japan **60**:76-78, Feb., 1956.

Ikeda, I., Komi, T., Nakaji, H. and Morikawa, H. **Characteristics of the nonspecific choroidal reaction.** *Ibid.* **60**:101-112, March, 1956.

The first part, a study of the change in adrenocortical lipids by repeated shocks which cause nonspecific ocular reactions, is reported. Intravenous injection of epinephrine, pilocarpine, and extract of liver and kidney were given daily to rabbits and such reactions as corneal opacity, choroidal hemorrhage and appearance of bubbles and clumps in the choroid about the blood vessels became manifest. The paranephros was removed serially for histochemical examination. During the stage of alarm reaction, unsaturated glycerid is chiefly found in the outer layer of fasciculata; during the stage of resistance in the middle and inner layer; and during the stage of exhaustion in the reticularis and in the inner layer of fasciculata.

In the second part, the authors state that an administration of sodium bicarbonate and vitamin C accelerates the manifestation of the nonspecific choroidal reaction. Yukihiko Mitsui.

Jaeger, W. and Winker, H. J. **Adsorption of mydriatics and miotics on artificial membrane.** Arch. f. Ophth. **156**:404-414, 1955.

The speed with which the more commonly used mydriatics and miotics are adsorbed onto an artificial membrane and their resistance to removal from it were measured. Among the mydriatics those which are sympathetic stimulants are more rapidly adsorbed and removed than the parasympathicolytics. The miotics which act by inhibition of cholesterinase are quickly washed off the membrane. (4 figures, 1 table, 7 references)

F. H. Haessler.

Karaki, S. **Changes in cellular structure of ocular tissues in the alloxan diabetic rabbits.** Acta Soc. Ophth. Japan **60**:251-280, April, 1956.

Karaki studied the lens and other ocular tissues in the alloxan diabetic rabbits with special reference to the changes in Golgi apparatus and metochondria. A degeneration of lens epithelium with subepithelial vacuolization at the equator takes place in the early stage of alloxan diabetes and is followed by a hypertrophic regeneration of the epithelium which causes cataract development. During the stage of degeneration an atrophy occurs and a disappearance of the Golgi apparatus with a deformation and reduction of mitochondria in the epithelial cells. The changes in the iris and ciliary body are slight and appear in the later stage in which the cataract develops. The changes in the retina and cornea are negligible. (37 figures, 73 references)

Yukihiko Mitsui.

Kawashima, K. **Measurement of the blood pressure of the central retinal artery by electric sphygmotonometer.** Acta Soc. Ophth. Japan **60**:38-45, Jan., 1956.

The blood pressure of the central retinal artery is calculated from the corneal pulse wave recorded by an electric sphygmotonometer. When the corneal pulse wave is recorded under an application of continuously increasing compression of the eyeball the change in the height of the corneal pulse wave clearly indicates the degree of compression corresponding to the diastolic and systolic blood pressure of the retinal artery. (7 figures, 10 references)

Yukihiko Mitsui.

Khasanova, N. **The neurological factor in the pathogenesis of chemical burns of the eye.** Vestnik oftal. **34**:12-17, Nov.-Dec., 1955.

In five rabbits the cornea was burned with ammoniates and in five with a 25-percent solution of sulphuric acid. The animals were killed in ½, 1, 3 and 24 hours after the instillation of the chemicals. There was destruction of sensory and trophic nerves which was more severe when the time after the instillation of the escharotics was prolonged. On this basis the author applied a novocaine blockade of the ciliary ganglion in 34 rabbits. Five rabbits burned with alkali and five with acid were given only local treatment. In 10 other rabbits a novocaine blockade was added within the first hour after the instillation of the escharotics. Ten rabbits were given local treatment combined with the novocaine blockade and in four rabbits the novocaine blockade was made a few minutes before instillation of the escharotics. The histopathologic examination showed that the burns of the cornea with local treatment only had a severe course with eventual perforation of the cornea or formation of leucomas and proliferation of blood vessels. In the rabbits in which the blockade was applied, the course was less severe and shorter and the opacities of the cornea were nebular.

On the basis of these experiments, 22 patients with alkali burns and 21 with acid burns were given a novocaine blockade, seven or eight times daily. The course of the disease was shorter, only five patients had a leucoma as an end result and in 18 patients there were nebular opacities of the cornea; in the others the cornea was transparent. The sensitivity of the cornea was absent long after the process of healing was complete in 10 patients with a severe alkali burn. (6 figures)

Olga Sitchevska.

Kittel, V. and Schubert, W. **The development of gas bubbles in the eye as a result of increased pressure.** Arch. f. Ophth. **156**:328-336, 1955.

In the anterior chambers of dogs, rabbits and guinea pigs which had been subjected to pressures of 20 atmospheres, gas bubbles were seen soon after the pressure was reduced to normal. Most of the animals were dead. Presumably the gas entered the animal by diffusion through the integument. (3 figures, 9 references)

F. H. Haessler.

Kuboki, T. **Electromyography of the human ocular muscles.** Acta Soc. Ophth. Japan **60**:29-37, Jan., 1956.

This is a study of the electromyograph by oscillography of the external ocular muscles with special reference to the electrical activity of each neuromuscular unit. During a slow horizontal movement of the eyeball, not only the prime mover, but also a few neuromuscular units in the antagonist exhibit electrical activity. Even a simple movement of the eye in horizontal direction is controlled by a complicated impulse complex. (19 figures, 19 references)

Yukihiko Mitsui.

Kuechle, H. J. **Experimental data for an optimal PAS therapy in ophthalmology.** Arch. f. Ophth. **156**:261-271, and 272-282, 1955.

In the first of these two articles and in an earlier one which appeared in 1952 the author reports the results of his studies of normal eyes. Therapeutically adequate concentration in the aqueous can be produced by instillation in the rabbit and even greater ones with the use of the eye cup. Particularly great concentrations follow the application of hypertonic solutions but concentrations of 15 to 25 percent lead to irreversible corneal damage. Cocaine did not increase the permeability of the cornea but mechanical injury to the epithelium did. Subcutaneous deposits of hyaluronidase was ineffective, but when this substance was given intravenously shortly before the intravenous injection of PAS, significant great quantities of PAS were found in the aqueous. In the

last report, experiments with inflamed eyes are described, which had the practical suggestion for PAS therapy in tuberculous lesions of the eye. (1 figure, 5 tables, 64 references) F. H. Haessler.

Leopold, I. H., Kroman, H. S. and Green, H. **Intraocular penetration of prednisone and prednisolone.** Tr. Am. Acad. Ophth. **59**:771-778, Nov.-Dec., 1955.

The authors show that the superior action of these two new corticoids in ocular therapy is not related to the degree of penetration into the aqueous humor of rabbits. (3 figures, 3 tables, 4 references) Theodore M. Shapira.

Leplat, G. and Gerebtzoff, M. A. **The localization of cholinesterase and the diphenolic mediators in the retina.** Ann. d'ocul. **189**:121-128, Jan., 1956.

Histochemical research on cat and rabbit retinas shows that the diphenolic mediators (adrenalin and noradrenalin) occur in the photosensitive cells, while cholinesterase is found in the internal plexiform layer. The rods and cones seem to be adrenergic and the bipolar cells cholinergic. This alternation of cholinergic and noncholinergic neurons is not continued further along the visual pathway, however, since the ganglion cells of the retina are also cholinergic. (2 figures, 37 references) John C. Locke

Lepri, G. and Fornaro, L. **Experimental tuberculosis and STH.** Gior. ital. oftal. **8**:516-526, Nov.-Dec., 1955.

The hormone of the anterior pituitary, STH, exerted a protective action on rabbits experimentally inoculated with tubercle bacilli. It limited the inflammatory processes and necrosis. (4 figures, 34 references) V. Tabone.

Mayer, G., Michaelson, I. C. and Herz, N. **Hyaluronidase in ocular tissues.** Brit. J. Ophth. **40**:53-56, Jan., 1956.

Several authors have reported finding hyaluronidase in considerable quantity in various ocular tissues. This is questioned by the authors who describe a sensitive test for its presence. In tissues of the iris, traumatized cornea, aqueous and ciliary body of the rabbit's eye, no appreciable amount of hyaluronidase was found. (3 figures, 9 references) Morris Kaplan.

Morone, G. **Glucosamine in the serum of patients with diabetic retinopathy.** Gior. ital. oftal. **8**:365-373, Sept.-Oct., 1955.

The serum concentration of glucosamine was estimated in 44 patients with diabetes. A correlation was found between retinal complications and high glucosamine levels in the blood. Insulin favorably influenced the concentration of glucosamine, and if the above correlation is of any significance, early therapy should also influence favorably diabetic retinopathy. (1 figure, 2 tables, 10 references) V. Tabone.

Naumann, Friedrich. **The resorbtion of certain drugs in the anterior chamber of the rabbit.** Arch. f. Ophth. **156**:293-302, 1955.

Various substances which are of importance in ophthalmology were introduced into the anterior chamber of rabbits by injection or implantation. Oily solutions are not absorbed, the oil finds its way to peripheral parts of the chamber and remains there for weeks or months without causing any reaction. Solutions of thrombin, thrombokinase, rutin and penicillin in saline solution are well tolerated. Undissolved thrombin and thrombokinase are soon absorbed but occasionally fibrinous nets remain on the lens. Undissolved penicillin is absorbed extremely slowly and gives rise to corneal opacification. Rutin called forth a very definite reaction. Gelatin sponge and dried lyophil are tolerated. The absorption of gelatin sponge is retarded when thrombin, throm-

bokinase or penicillin is added to it. When collargol is added to gelatin sponge, the sponge is absorbed but the collargol or precipitated silver remains. Gelatin sponge with rutin gave rise to minimal transient opacification of the cornea but absorption was very slow. (5 references)

F. H. Haessler.

O'Rourke, J. F., Iser, G. and Ryan, R. W. **An initial evaluation of prednisone therapy in ocular inflammation.** A.M.A. Arch. Ophth. **55**:323-332, March, 1956.

The authors report their experimental and clinical studies of prednisone. They found it to be five times as effective as the other steroids, although not useful in any more entities. As expected, it was of most value in acute anterior lesions. No significant side effects were observed in patients treated daily for over three months with prednisone. (5 figures, 3 tables, 7 references)

G. S. Tyner.

Pentini, G. and Scassellati Sforzolini, G. **Effect of hydrocortisone on experimental corneal lesions.** Gior. ital. oftal. **8**:374-382, Sept.-Oct., 1955.

The local application of both cortisone and hydrocortisone delayed repair of corneal wounds. Both drugs acted similarly, and the final cicatrization was normal in all respects. The authors conclude that the drugs could be used locally with safety, provided the dose and its frequency are not excessive. (23 references)

V. Tabone.

Popp, Claus. **Retinal function after intraocular ischemia** Arch. f. Ophth. **156**: 395-403, 1955.

The ERG was used as an index of recovery of retinal function after retinal ischemia and four degrees of recovery were noted which were associated with the duration of the ischemia. After ischemia for 15 minutes recovery was complete. Conditional recovery, which occurred after ischemia for 30 to 75 minutes, was characterized by defects in the ERG which gave way to complete recovery after one to ten days. After ischemia for 60 to 90 minutes complete recovery is not permanent and after an ischemia lasting 105 minutes there is no bioelectric evidence of a return of vision. (3 figures, 2 tables, 15 references)

F. H. Haessler.

Radnót, M. and Orbán, T. **Effect of light on thyroid function.** Szemészet **1**:1-3, 1956.

In ducks light enhances thyroid activity. Continuation of illumination results in thyroid hyperactivity. The animals lose weight and become irritated, the function of the gonads decreases and signs of degeneration occur. Light acts on the neuroendocrine apparatus through the eye.

Gyula Lugossy.

Remky, Hans. **Adjustment of the cerebral circulation to normal exertion. Its experimental demonstration through the intermediary of the retinal circulation.** Ann. d'ocul. **188**:849-857, Sept., 1955.

The method of Bailliart (Ann. d'ocul. 154:648, 1917) is used to measure alterations in retinal arterial pressure, occurring: 1. on changing from a sitting to a lying-down position; 2. on movement of the head; and 3. during static and dynamic exercise. Parallel changes are assumed to occur in the cerebral circulation. In young people, change from a sitting to a lying-down position causes an increase in retinal arterial pressure lasting up to two hours. With increasing age, this effect becomes gradually less, and in older people the opposite effect is found. Adrenergic drugs lessen the increase found in the younger subjects, suggesting that an excessive rise signifies decreased vascular tone, while a small or negative change indicates hypertension. Supporting a weight on the forearm causes an immediate increase in both diastolic and systolic retinal arterial pres-

sures. Rotating the head causes a sudden unilateral rise. (6 figures, 13 references)

John C. Locke.

Rezanov, P. **The role of the central nervous system in the permeability of the vessels of the eye.** Vestnik oftal. **34**:3-6, Nov.-Dec., 1955.

In three series of experiments the author used the method of labelled molecules instead of the colorimetric and histologic methods.

In the first series of experiments (90), depression of the nervous system was obtained by introduction of veronal into the stomach of the rabbit. Stimulation of the nervous system was obtained by subcutaneous injections of caffein (1-percent solution). The therapeutic sleep produced by the veronal caused a decrease and the stimulation of the nervous system caused an increase of the permeability of the eye vessels.

In the second series the condition of the permeability of the vessels was studied in depressing and exciting the central nervous system by removal of the superior cervical sympathetic ganglion on one side. In five rabbits, the ganglion was removed during the waking hours, in five after the period of depression and in five during the period of stimulation. The aqueous was removed (after the phosphorus had entered the anterior chamber) and studied. The sympathectomy in the period of depression of the central nervous system was followed by a slight increase of the permeability of the vessels, but it was greatest during the period of the stimulation of the nervous system. In all rabbits the permeability of the vessels was decreased in the other eye (where no sympathectomy was done) and this was probably due to a reflex influence.

In the third series, 20 experiments were done; 0.3 mg. of 10 percent solution of salt was injected subconjunctivally in the period of depression and stimulation. The aqueous was examined an hour after the injection. There was no increase in the permeability in the period of depression but it was greatly increased during the period of stimulation.

A unilaterial sympathectomy was done on five rabbits which was followed by a subconjunctival injection of hypertonic salt solution on the same side. An increase of the permeability of the vessels occurred on the side of the sympathectomy.

All these experiments indicate that the permeability of the vessels of the eye is regulated by the central nervous system. It is possible that the impulses are transmitted by the trigeminal nerve and by some neurohumoral mechanism. (3 tables)

Olga Sitchevska.

Rizzini, Vittorio. **Sodium and potassium in the aqueous and lens of the rabbit.** Gior. ital. oftal. **8**:461-469, Nov.-Dec., 1955.

In a series of experiments on rabbits' eyes the values for sodium and potassium concentration in the aqueous and lens, obtained with the flame spectrophotometer of Beckman, were compared with those obtained by other methods. While the values for the aqueous were similar, those for the lens were different. The effect of ACTH and cortisone on the sodium and potassium concentration in the aqueous and lens was also studied. The former produced a change in the electric equilibrium and an inversion of the sodium-potassium ratio, the latter had only doubtful effect. (1 table, 21 references)

V. Tabone.

Schwarz, V. and Golberg, L. **Galactose 1-phosphate in galactose cataract.** Biochim. et Bioph. Acta **18**:310-311, 1955.

Young male albino rats (initial weight 50 to 60 g) were fed a diet containing 30 percent of galactose; controls were given the same diet without galactose. After varying intervals the animals were killed

and the lenses excised. It was found that: 1. control lenses or capsules contain a maximum of 0.08 μg Ga 1-P per capsule, 2. whole cataractous lenses contain approximately the same amount of Ga 1-P as do separated capsules, i.e. approximately 1 μg per capsule, and 3. capsules of noncataractous lenses from galactose-fed animals contain amounts of Ga 1-P similar to those found in normal lenses. The lenses were not examined histologically, but there were no opacities visible to the naked eye. (8 references)

F. H. Haessler.

Suedhof, H. and Schweer, G. **Glucosamine of the vitreous.** Arch. f. Ophth. **156**: 427-432, 1955.

A reliable method for the determination of glucosamine in the vitreous is described. This method is preferred to other methods because it provides simpler yet precise neutralization of the dialysates and a constance of the photometric color value. The differences in values found can probably be ascribed to the age of the animal and will be the subject of a subsequent communication. (16 references)

F. H. Haessler.

Takaoka, S. **Change in the intraocular pressure and K-ion concentration in serum and aqueous by diamox and adrenalin.** Acta Soc. Ophth. Japan **60**: 232-251, and 281-284, April, 1956.

In rabbits an increase in concentration of K ions in the blood and the aqueous is brought about by the administration of adrenalin, while a decrease is brought about by diamox. Both agents, however, cause a decrease in ocular tension. Ocular tension and K-ion concentration do not seem to be correlated. It is interesting to know, however, that in glaucoma in which a single administration of diamox results in a continuous lowering of ocular tension, the decrease in K-ion concentration persists for 16 to 27 hours, that is, beyond the period of persisting effect of diamox. (6 figures, 16 tables, 105 references)

Yukihiko Mitsui.

Tanaka, J. **Influence of autonomic drugs upon intraocular lymphatic streams.** Acta Soc. Ophth. Japan **60**:78-91, 91-104, and 173-175, Feb. and March, 1956.

By an injection of atropine into the vitreous or subconjunctiva, the migration of India ink through the anterior and posterior lymphatic pathways of the eye is suppressed; and the converse occurred after an injection of benzyl imidazoline. (26 figures, 15 tables, 102 references)

Yukihiko Mitsui.

4

PHYSIOLOGIC OPTICS, REFRACTION, COLOR VISION

Ahlenstiel, Heinz. **Blue spots as a pathologic entoptic phenomenon.** Klin. Monatsbl. f. Augenh. **128**:203, 1956.

The author, a 64-year-old physician with vascular hypertension, notices occasionally blue spots in his eyes when light strikes him in a darkened room. He assumes that it is caused by a venous stasis and capillary dilatation in the retina. (4 references)

Frederick C. Blodi.

Allen, Merrill J. **The influence of age on the speed of accommodation.** Am. J. Optometry **33**:201-208, April, 1956.

If the strength of the ciliary muscle remains the same in presbyopia, efforts at accommodation should either cause excessive convergence or there should be a decrease in the accommodation convergence ratio. Neither of these possibilities has been reported to occur.

In this paper the subject of speed of accommodation was reviewed, and tested on 14 subjects aged 7 to 49 years. The time for accommodation was found greater than time required for the relaxation of accommodation. There appeared to

be no correlation of speed of accommodation with the accommodation-convergence ratio. Paul W. Miles.

Bangerter, A. **Are the results of amblyopia treatment misleading?** Klin. Monatsbl. f. Augenh. **128**:182-186, 1956.

The success of treatment of patients with amblyopia depends upon the improvement of the visual acuity. Taking visual acuity in children takes patience, understanding and alertness. It is often better done by the orthoptic technician. When measuring the visual acuity of an amblyopic eye two recordings should be done. One is obtained when exposing single letters and another is made by reading letters in a row.

Frederick C. Blodi.

Bannon, Robert E. **Physiological factors in multifocal corrections. Part II. Considerations of optical functions and patient's needs.** Am. J. Optometry **33**:171-188, April, 1956.

This paper states in simple terms the problems involved in first bifocals. Patients who have been in the habit of wearing glasses full time have little complaint with first bifocals, while those who are only slightly ametropic have trouble. It is wise to say, "In a year you may be ready for bifocals, but for right now, two pairs are suggested." It is common, but wrong, for patients to wait until they need +1.00 diopter reading addition, because at any time a change of +.50 diopters should be significant. Temporary bifocals in round frames may be loaned to help patients make up their minds on first trial. Various types of available bifocal forms are described. Straight top or "cut-off" segments are recommended to reduced image jump and object displacement.

When a patient has occupational requirements, do not hesitate to advise special form glasses. One should prescribe "arm's length plus a tool." Overhead near work requires a stronger addition than work in the reading position at the same distance.

Trifocals should be prescribed in most cases when the reading addition is +1.75 or more. It is psychologically objectionable to prescribe new bifocals and advise old bifocals for arm's length tasks. The patient's habitual posture must be matched in the segment height and position. Measurement of refraction is a science, but prescription of lenses is an art.

Paul W. Miles.

Bensusan, Jose Ribas. **The clinical aspect of cylindrical ametropia.** Arch. Soc. oftal. hispano-am. **15**:1159-1166, Oct., 1955.

Bensusan discusses the types of astigmatism, and the effect of accommodation on each type. Ray K. Daily.

Berger, Curt. **Visual acuity decrease at various illuminations and role of reading.** A.M.A. Arch. Ophth. **55**:408-412, March, 1956.

On the principle of muscular experiments, in which the weight lifted is both the measure and the cause of fatigue, a cumulative and significant decrease of visual acuity (average slope about 18 percent) in the course of repeated series of monocular measurements with Landolt's broken circle is described. There was no consistent effect of level of illumination upon the measured decrease of visual acuity. The possible relation of these facts to the etiology of myopia is discussed. (2 figures, 10 references) G. S. Tyner.

Etienne, Raymond. **The cylinder rotation test in retinoscopy.** Ann. d'ocul. **188**: 904-919, Oct., 1955.

The author reviews in detail the cylinder rotation tests of Lindner and Kraemer and emphasizes their value in determining cylinder axis and power in retinoscopy. (4 figures, 12 references)

John C. Locke.

Franceschetti, A. **The prescribing of prisms, particularly those at oblique axes.** Ann. d'ocul. **189**:137-151, Jan., 1956.

A combined vertical and horizontal deviation can be corrected by a prism with a vertical axis on one side and a prism with a horizontal axis on the other. It is preferable, however, to prescribe prisms with oblique axes for the two eyes. The value of Allen's chart (Arch. Ophth., 22:113, 1939) in estimating the required strength and axis of oblique prismatic corrections is emphasized. (6 figures, 11 references)

John C. Locke.

François, J. and James, M. **Comparative study of the treatment of amblyopia ex anopsia.** Ann. d'ocul. **188**:827-833, Sept., 1955.

Two groups of 100 amblyopic patients, chosen at random from 1,800 with strabismus, are compared. The first group has been treated by occlusion only and the second by occlusion combined with visual stimulation. The end results are the same, but the time taken to achieve maximal vision is greatly reduced by means of occlusion and exercises combined. In four weeks, 68 percent of the second group reached maximal vision, whereas it required 14 weeks for 69 percent of the first group to reach this maximum. (1 figure)

John C. Locke.

Frey, R. G. **Changes in refraction after scleral excision.** Arch. f. Ophth. **156**:313-322, 1955.

Theoretic consideration of the effect of scleral excision on an eye, which is schematically thought of as a sphere, hardly leads one to expect the development of hypermetropia. The change in diameter brought about by this operation is slight and other effects of the operation (increased curvature of the cornea and advancement of the lens) could lead one to expect at least partial neutralization of the effect of shortening the antero-posterior diameter of the globe. Where scleral shortening is limited to segments of the circumference the development of corneal astigmatism might be expected.

A study of the effect of 42 operations on 32 eyeballs with retinal detachment showed that in one third of the eyes the refraction was unchanged. In another quarter there was a change of refraction up to 1.75 diopters and almost always toward hypermetropia. In almost two fifths of the eyes the increase of hypermetropia was greater than two diopters. In one there was a permanent reduction of myopia of 5.5 diopters. There was no direct relationship between the distance of the excision from the limbus or its width and the change in refraction. The total astigmation ascribable to the operation averaged 2.3 diopters. Scleral resection may have a favorable secondary effect in myopic eyes with retinal detachment, whereas an undesirable development of hypermetropia need not be anticipated with certainty. In aphakic originally myopic eyes, however, hypermetropia may develop. Postoperative astigmatism occurs within the limits expected after cataract extraction. (7 tables, 9 references)

F. H. Haessler.

Fry, Glenn A. **The discrepancy between physical and perceived curvature.** Am. J. Optometry **33**:147-154, March, 1956.

This is a mathematical discussion of binocular depth perception based on a rectilinear representation of the horopter compared to subjective data. Relative distances of objects in space are determined by physiological processes in the brain related to retinal binocular image disparity and on size constancy. The latter is particularly true in the case of moving objects changing in visual angle. Essentially, the job which the brain must perform is to associate with each distance of binocular fixation, a surface of a certain curvature representing the counterpart of

the horopter in visual space. Then objects in front of or behind the horopter are perceived in relation to the counterpart of the horopter in visual space.

Paul W. Miles.

Granger, G. W. **Dark adaptation time in neurotic patients.** Brit. J. Physiol. Optics **13**:39-44, Jan., 1956.

Neurotic patients do not dark adapt readily after exposure to a light. In an accepted test for dark adaptation, 50 neurotic patients required an average of 24 seconds to perceive the target whereas an average of 20 seconds was required by 40 normal subjects. Both groups were selected to include both sexes and all age groups. The test would be suitable for testing large groups of people.

Paul W. Miles.

Gyoerffy, I. **Correction of unilateral aphakia by means of contact lenses.** Ophthalmologica **130**:329-335, Nov., 1955.

Contact lenses were given to 25 subjects with monocular aphakia with normal visual acuity of the fellow eye and 16 of them became regular wearers of contact lenses. In 20 cases binocular vision was restored. "Although we have in view a new and perhaps better procedure—replacement or implantation of the lens by the method of Ridley—the contact lens remains meanwhile the method of choice to correct monocular aphakia." (10 references) Peter C. Kronfeld.

Hammer, J. **Permanency of amblyopia treatment?** Klin. Monatsbl. f. Augenh. **128**:195-199, 1956.

Two hundred eight patients who were originally treated for amblyopia could be re-examined at an average of 3.4 years later; 53 percent of the patients remained unchanged, 20 percent showed continuous improvement. The 27 percent of the patients who had regressed were successfully retreated. (6 figures, 4 references)

Frederick C. Blodi.

Ishtwan, D. **The use of contact lenses for the improvement of vision.** Vestnik oftal. **34**:25-32, Nov.-Dec., 1955.

A historical review, a description of the various contact lenses, the technique of the trial, and a description of the uses, indications, contraindications of contact lenses are given by the Hungarian ophthalmologist. Olga Sitchevska.

Manas, Leo. **Cheiroscopic drawing: target modification for maximum training benefits.** Am. J. Optometry **33**:113-117, March, 1956.

Cheiroscopic drawing is valuable for breaking down suppression, reducing amblyopia, and improving fusion, but the patient's tropia interferes. In esotropia, the target must be tall and narrow, while in exotropia, the most effective target is large and round. The pencil should be on the side of the amblyopic eye.

Paul W. Miles.

Morrison, L. C. **Further observations on stereopsis in the presence of diplopia.** Brit. J. Physiol. Optics **13**:10-14, Jan., 1956.

Three light points were arranged in a frontal plane, the two outer ones being polarized at right angles to each other. With the central point for fixation, a subject wearing polaroid lenses would see the right point with the right eye and left point with the left. Keeping the angular values within 20 minutes of arc and thus within Panum's fusional areas, there was not consistent discrimination of relative distance of the lateral objects from fixation. The lights were exposed only .06 seconds. When this exposure time was prolonged, the points were seen in crossed or uncrossed disparity according to the position of the polaroids, with depth value near or distant. One subject was able to discriminate depth under these conditions with .06 seconds exposure, even when the

disparity was increased beyond the point of noticeable diplopia. Paul W. Miles.

Morton, R. **Myopia: the present position.** Brit. J. Physiol. Optics **13**:15-24, Jan., 1956.

The etiology of myopia remains unknown. All we can tell the parents is that we hope it will not increase rapidly, and that the glasses may help. The recent work in X-ray determination of axial length of the globes has been valuable, but should be done in small children repeatedly during the development of myopia. Such a subjective test would be difficult in a child.

Various theories of myopia are discussed. The mistaken ideas of Bates that the oculorotary muscles are "lazy" and need exercise must not be allowed to close our minds on the subject. Morton would like to see some controlled studies on the effect of exercises to prevent myopia before it leaves the hypermetropic stage. Certainly undercorrection of glasses cannot help, because all myopia develops from hypermetropia without the effect of glasses. Children in the schools should be prevented from reading fine print at short visual distances. Paul W. Miles.

Ohm, Johannes. **Proprioceptive stimulation of the retina.** Arch. f. Ophth. **157**:211-224, 1956.

The author studied this phenomenon in himself. He found that after prolonged exposure to darkness the proprioceptive retinal stimuli overshadow the sensitivity of the fovea and the perifoveal district to light stimuli otherwise just noticed. Long ago the author had made the assumption that proprioceptive retinal stimuli were involved in the production of the nystagmus of darkness. This assumption was confirmed by other authors' experiments. The present study lends further evidence to the author's views on this type of nystagmus. (3 references)

Ernst Schmerl.

Schapero, Max. **Aniseikonia due to changes in corneal curvature caused by dendritic corneal ulcer—a case report.** Am. J. Optometry **33**:196-200, April, 1956.

A pilot, aged 34 years, developed 0.75 diopters of astigmatism in one eye after a dendritic ulcer. This caused poor depth perception which was relieved by glasses correcting the astigmatism and the aniseikonia: × 90 right eye .50 percent; × 180 right eye 2.5 percent; oblique 0.0.

After a few months, the ulcer recurred. The astigmatism increased to 3.75 diopters, and the aniseikonia increased to: × 90 right 7.5 percent; × 180 right 1.5 percent; oblique +.3. The space distortion was extreme. While it could be corrected by cylindric and aniseikonic lenses, with an acuity of 20/40; this was not considered advisable. Five percent magnification is all that can be prescribed with any cosmetic acceptance.

Paul W. Miles.

Tinker, Miles A. **Effect of sloped text upon the readability of print.** Am. J. Optometry **33**:189-195, April, 1956.

Three hundred university students were tested in reading speed and comprehension of printed matter of 10 and 8 point type tilted to various degrees. There was a decrease of 5 to 10 percent with a book laid flat on the table compared to a position perpendicular to the visual line.

Paul W. Miles.

5

DIAGNOSIS AND THERAPY

Bandurski, A. and Chwirot, R. **A rare case of post-traumatic arterio-venous fistula of the large vessels of the neck.** Klinika Oczna **25**:49-58, 1955.

A case of post-traumatic arteriovenous fistula between the right external carotid artery and the jugular vein in a man, 39 years of age, is described. The vein was almost completely closed which prevented hypertrophy of the heart and venous con-

gestion. Five years after injury cyanosis and edema of the right side of the face and increased intracranial pressure appeared. There was only slight exophthalmos on the same side with congestion and tortuosity of conjunctival veins. The disc looked normal. There was papilledema on the left side only and the author believes that this is pathognomonic of this morbid picture. Surgical removal of the fistula resulted in recession of all these symptoms. (6 figures, 32 references)

Sylvan Brandon.

Beiras, Antonio. **A clinical note on slit-fundoscopy.** Arch. Soc. oftal. hispano-am. **15**:1271-1275, Nov., 1955.

The author describes a modification of the Oculus ophthalmoscope, which affords a satisfactory examination of the fundus with a slit. The modification consists in making two additional observation openings on each side of the mirror which reflects the light into the fundus. This brings about a very acute angle between the axis of the incident ray of the illuminated slit and the optic axis of the observer's eye. The instrument as manufactured gives no depth relief of the fundus. The modified ophthalmoscope affords a view of the fundus in which differences of level stand out sharply, the illuminated quadrangle area being in sharp contrast with the darker color of the adjacent fundus. (3 figures)

Ray K. Daily.

Cambiasso, Raul Hector. **Preliminary report on the results of chorionic gonadotrophin administration in cases of progressive myopia and of incipient keratoconus.** Arch. oftal. Buenos Aires **30**:391-402, Oct., 1955.

The contention that the appearance and development of degenerative, or pathologic, myopia and of conical cornea are due to a disturbance of the function of the pituitary gland by which the growth of the fibroplastic tissues of the body is governed, is not new and seems to be supported by some clinical facts. Yet, its natural corollary, the use of gonadotrophic substances in order to check the progression of these anomalies, has never found much acceptance. To determine whether such treatment is really of some avail, the author administered chorionic gonadotrophin for a period of several months to two patients with mild keratoconus and to 16 with progressive myopia of a most variable degree. Some of these myopias undoubtedly were mere biologic variants, while others were certain instances of the so-called degenerative form of the defect. The results were invariably good, in that the refractive error either ceased to increase or actually decreased slightly; these encouraging conclusions were mostly based upon subjective measurements of visual acuity rather than on objective determinations of the axial length of the eye and of the total refractive power or its optical components. (1 graph)

A. Urrets-Zavalia, Jr.

Colenbrander, M. C. **A new test type.** Ophthalmologica **130**:219-220, Sept., 1955.

The new chart is made up of the letters B, E, H, K, N, R and S, drawn so as to be equally difficult and equally confusable. Optotypes meeting these requirements are more difficult to recognize than those of the conventional Snellen chart and, therefore, have to be made about 10 percent larger than the latter in order to yield the same visual acuity.

Peter C. Kronfeld.

Dekking, H. M. **An instrument for measuring visual power.** Ophthalmologica **130**:225-226, Sept., 1955.

The efficiency of the visual apparatus expresses itself not only in the visual angle subtended by the smallest detail perceived, but also in the degree of contrast between these details and their sur-

rounds, in the average brightness of the test field and in the length of time necessary for perception of the details of the test object. The author has designed a portable instrument for the measurement of visual acuity under variable contrast and overall brightness conditions.

Peter C. Kronfeld.

Fehse F. and Straub W. **Microprojection and its uses.** Arch. f. Ophth. **157**:294-301, 1956.

A special apparatus for the projection of microscopic objects is described. (16 figures, 7 references) Ernst Schmerl.

Foster, John. **Ophthalmic needle holder.** Brit. J. Ophth. **40**:60-61, Jan., 1956.

The author describes a modification of the Gillies needle holder. The jaws have finer serrations for holding the new smaller corneal needles and there is a flat space at the tip of the jaws for grasping sutures when tying. (1 figure, 1 reference) Morris Kaplan.

Galvez Montes, J. **A simplified method of electronystagmography.** Arch. Soc. oftal. hispano-am. **15**:1299-1310, Dec., 1955.

The author describes a method of using an electrocardiograph for registering the ocular movements. He designed a headband with attached electrodes for their easy and simple application to the globes. (14 figures) Ray K. Daily.

Gerkowicz, Kazimierz. **Preventive topical use of aureomycin before surgery.** Klinika Oczna **25**:15-20, 1955.

The author used aureomycin in treating the eyes of 25 patients in whom cultures taken during pre-operative preparation or after the operation revealed a penicillin-resistant strain of straphylococcus aureus. The conjunctival sac became sterile in 3 to 5 days and the drug caused no irritation. (2 tables, 8 references)

Sylvan Brandon.

Hogan, M. J., Thygeson, P. and Kimura, S. **Effects of prednisone and prednisolone in ocular inflammation.** Tr. Am. Acad. Ophth. **59**:779-782, Nov.-Dec., 1955.

Prednisone and prednisolone solutions, 0.5 percent, are as effective as hydrocortisone acetate, suspension, 2.5 percent, in controlling surface lesions of the conjunctiva and cornea when applied topically. Weaker solutions are not as effective. Intraocular inflammations are controlled equally well by the oral administration of these agents, when compared with hydrocortisone and cortisone, and a lower dosage is required. Experimental herpes febrilis infections of the cornea were more severe and the incidence of subsequent encephalitis was higher than in the controls when rabbits were given prednisolone, 8.0 mg. subconjunctivally. The results were almost identical to those obtained with hydrocortisone and cortisone. This would suggest that topical therapy with these agents might be expected to activate latent herpes febrilis infections in the same manner as hydrocortisone has done. No instance of activation, however, was detected in over 200 treated cases. (2 tables, 1 reference)

Theodore M. Shapira.

King, J. H., Passmore, J. W., Skeehan, R. A., Jr. and Weimer, J. R. **Prednisone and prednisolone in ophthalmology.** Tr. Am. Acad. Ophth. **59**:759-770, Nov.-Dec., 1955.

The authors produced experimental uveitis in rabbits and applied these two new corticoids therapeutically. These drugs are valuable in all ocular diseases which have responded to cortisone and hydrocortisone because of the absence of toxic side effects. The authors think that these newer drugs will replace hydrocortisone for severe inflammation requiring oral therapy because of its greater superiority in achieving full effect of the

adrenal corticosteroid. (5 figures, 5 tables, 7 references) Theodore M. Shapira.

Kisseleva, B. **The opsonin phagocytosis reaction in the diagnosis of brucellosis infection of the visual organ.** Vestnik oftal. **34**:17-19, Sept.-Oct., 1955.

The technique of this test is described: it was positive in 33 of 35 patients with chronic brucellosis and in 22 of 25 children with various tuberculous affections of the bones and joints.

Olga Sitchevska.

Lepri, G., and Andreani, D. **Diamox in nonglaucomatous eyes.** Gior. ital. oftal. **8**:499-504, Nov.-Dec., 1955.

The drug was tried in various nonglaucomatous disturbances in the eye, with mostly negative results. (19 references)

V. Tabone.

Merriman, George R., Jr. **Effects of beta radiation on the eye.** Radiology **66**:240-245, Feb., 1956.

There has been no uniformity of expression of dosage. It is hoped that the roentgen equivalent physical (rep) will be adopted as the standard dosage unit for beta radiation. Telangiectasis of the conjunctiva has been observed to appear about five years after the completion of therapy using doses of 3,000 to 5,000 rep. Keratinization of the conjunctival epithelium has followed doses of 5,000 to 10,000 rep. Doses of 20,000 to 30,000 rep have produced atrophy of the sclera; corneal vascularization (eight to ten years after therapy); corneal scarring (two to five years after therapy); iris atrophy and radiation cataract (three to thirteen years after therapy).

It is suggested that the current high schedules be reduced. Doses of 2,000 to 3,000 rep on the surface would be judicious and that a surface dose of 5,000 rep should seldom be exceeded in the treatment of benign lesions. (1 table, 23 references) Irwin E. Gaynon.

de Muelenaere, H. **The synoptophore.** Ann. d'ocul. **188**:1042-1058, Nov., 1955.

The synoptophore, its slides and accessories, are described in detail. Directions for its use in the investigation of binocular vision are reviewed. (6 figures)

John C. Locke.

Munoz, Luis. **Gelatinoids of fluorescein.** Arch. Soc. oftal. hispano-am. **15**:1246-1247, Nov., 1955.

The author designed a thin gelatinoid tablet impregnated with fluorescein, with methylcellulose as a solvent, which after being introduced into the conjunctival sac is rapidly dissolved by the tears. The author finds it more convenient for staining corneal abrasions than the fluorescein impregnated filter paper, which sometimes leaves shreds of paper in the conjunctival sac. (2 references) Ray K. Daily.

Neame, H. **Shade attached to spectacle frame to protect from glare in early or premature cataract.** Brit. J. Ophth. **40**: 61, Jan., 1956.

A shade which is attached to the upper rim of spectacles to protect photophobic patients from glare is briefly described. (1 figure) Morris Kaplan.

Niesel, P., and Leonardi, F. **Calibration of the Baurmann's angiotonometer and Mueller's ophthalmodynamometer.** Ophthalmologica **130**:295-311, Nov., 1955.

Both instruments are dynamometers in that they raise the intraocular pressure, by external pressure, to levels at which the characteristic gross pulsation phenomena occur in the retinal arterioles. In Mueller's instrument, as in Bailliart's original instrument, a spring-driven piston indents the eyeball wall and thereby raises the intraocular pressure. Baurmann accomplishes this by means of a small rubber balloon, filled with saline solution and connected with a manometer.

The pressure-raising effect of the two

instruments was measured on human cadaver eyes in situ by means of a manometer connected with a cannula in the anterior chamber. The same method of calibration was used on three living, tumor-bearing eyes, again in situ.

Baurmann's instrument proved superior to Mueller's instrument in that the readings agreed more closely with those obtained by manometry and showed less of a spread from one eye to another. Mueller's instrument, however, was handier and particularly so at higher pressure levels. (9 figures, 4 tables, 14 references)

Peter C. Kronfeld.

Oláh, I. **Basis and clinical application of electroretinography.** Szemészet **4**:176-183, 1955.

The characteristic deflections of the electroretinogram are the downward deflection a, the upward deflections b, c, d, resulting from the positive components P I and P II, and the negative P III. From a clinical point of view, the most important item is the analysis of deflection b, its differences being characteristic for individual diseases. Apart from the combination of ERG with perimetry or electroencephalography, ERG is a proper method for the objective determination of eye movements, movements of the pupil, and fusion frequency. Guyla Lugossy.

Payrau, P., Guyard, M. and Perdriel, G. **Isoniazid in ocular tuberculosis.** Ann. d'ocul. **188**:734-745, Aug., 1955.

The authors used isoniazide alone in eight cases of tuberculous uveitis (5 mgm. per kilo body weight per day). Complete cure was obtained in seven cases, the eighth patient being still under treatment. Response was more rapid in cases of anterior uveitis, but within an average period of two months choroidal lesions also became inactive. There were no untoward effects ascribable to drug intolerance. Four patients have been observed for from one to three months with no recurrence. (16 references)

John C. Locke.

Pettinati, Sergio. **Radiography of the optic canal.** Rassegna ital. d'ottal. **24**:381-390, Sept.-Oct., 1955.

Pettinati reviews the methods of many radiologists in picturing clearly the optic foramen. From an experience of some 2,000 radiograms he describes the method which has given him the best results. He stresses three steps in technique to obtain a clear round opening of the canal: 1. the central ray of light must be perpendicular to the plane of the film, 2. the central ray must coincide with the axis of the canal or the opening will appear to be oval, and 3. the image of the foramen must fall on the infero-external quadrant of the orbit. (5 figures, 21 references)

Eugene M. Blake.

Priestley, B. S. and Foree, K. **A new entoptoscope.** A.M.A. Arch. Ophth. **55**: 415-416, March, 1956.

The authors describe a new entoptoscope for the observation of Scheerer's phenomenon, which can be used not only for clinical observation but also for the study of sedatives and peripheral vasodilators and their comparative pharmacodynamic action on the retinal circulation. (2 figures, 1 reference) G. S. Tyner.

Rapisarda, Dante. **Effect of some hypotensive drugs on the retinal circulation and their therapeutic uses.** Gior. ital. oftal. **8**:426-445, Sept.-Oct., 1955.

The results on 40 patients are described. Apresolin, nepressol, serpasil and pendiomid were given by mouth, separately and in various combinations. The reduction of the systemic arterial pressure was usually reflected in the retinal vessels; the greatest reduction in the latter was procured by the combination of serpasil and pendiomid. Reduction of pressure in the

retinal vessels was correlated with rapid absorption of retinal hemorrhage and papilledema, as well as with improved visual acuity. Vascular and degenerative changes in the retina remained unchanged. (5 tables, 37 references)

V. Tabone.

Sachsenweger, Rudolf. **Examination of the central visual field.** Klin. Monatsbl. f. Augenh. **128**:167-172, 1956.

A polaroid campimeter is described. Polaroid filters make the fixation point visible to both eyes while the test target is seen by one eye only. The room must be darkened. The size of the fixation mark and the target can be varied. (4 figures, 1 table, 14 references)

Frederick C. Blodi.

Schiff-Wertheimer, S., Delahaye, G., and Dervieux, A. **Curarization without general anesthesia in the surgery of the lens.** Presse Med. **64**:253-255, Feb. 11, 1956.

The authors prepared over 200 patients for cataract surgery with the usual preoperative medications. Cocaine was instilled topically, a retrobulbar injection given, and the lids immobilized by infiltration. At this point one of three curare preparations was given intravenously. The authors give a long list of indications, general and local, for the use of curare which may be summarized by stating that the proposed extraction of anything except a simple senile cataract is an indication for curare. They find that the best preparation is the dimethyl chlorohydrate of methyl bebeerine (auxopéran). David Shoch.

Sedan, Jean. **In defense of dionine.** Ann. d'ocul. **188**:746-766, Aug., 1955.

Dionine, which used to be an essential drug in ophthalmology, has gradually fallen into disuse and is now almost unknown by most ophthalmologists. After reviewing its pharmacologic actions, the author describes its beneficial effects in a number of important eye diseases. While it is helpful in many conditions of the cornea, it has its greatest value in uveitis and congestive glaucoma. The discovery of cortisone only serves to enhance its usefulness. Since the effectiveness of both cortisone and dionine tend to decrease after prolonged use, it is fruitful to alternate periods of treatment with each of these two drugs. (101 references)

John C. Locke.

Smirnov, S. **A new scleral projector.** Vestnik oftal. **34**:32-37, Sept.-Oct., 1955.

A new simple scleral projector, for use in the localization of intraocular foreign bodies and in detachment of the retina as well as the necessary calculations are described in detail by Smirnov. (2 figures, 1 table) Olga Sitchevska.

Tahara, S. **Therapy of sea- and car-sickness by eye lotion.** Acta Soc. Ophth. Japan **60**:147-151, March, 1956.

Seven clinic patients and 195 students who are apt to suffer from seasickness were the subject of these experiments. A 0.5 or 1.0 percent solution of pilocarpine was instilled into the eyes of the subjects 20 minutes before travelling. In 86 percent of the cases the sickness was prevented. The effect of a single instillation seems to last for 12 hours and therefore a single application every day during a trip may be sufficient to prevent the sickness.

A slight astigmatism is often a cause of the sickness. In such cases, the correction of the error of refraction is more effective than pilocarpine as a preventive. (4 references) Yukihiko Mitsui.

Thomas, C. I. and Krohmer, J. S. **A transilluminator for use with the curved Geiger counter.** A.M.A. Arch. Ophth. **55**: 413-414, March, 1956.

To obtain satisfactory radioactive counts over an intraocular lesion, the mica window of the counter must be placed as nearly over the tumor as possible. A combination transilluminator and Geiger counter has been devised to be inserted through the conjunctival sac so as to facilitate the desired proximity. (1 figure, 2 references) G. S. Tyner.

Torrents, E., Cervino, J. M., Ravera, J. J., Saralegui, J. P. and Mussio Fournier, J. C. **Alterations in the electroretinogram in hyperthyroid states.** Presse Med. **64**:4, Jan. 4, 1956.

Electroretinograms were made for three hyperthyroid patients before and after treatment (surgical in two and radioactive iodine in the third). Generally there was an elevation of the b-wave potential from a normal of about 0.40 mV to a level between 0.48 to 0.70 mV. (The reverse is true in myxedema.) In both states there is an increase in the duration and latent period of the b wave. Treatment of the hyperthyroidism produced a reduction in these values. The authors feel that the number of cases studied is too few to draw any conclusions. David Shoch.

Wachter, H. E. and Pennoyer, M. M. **Prophylaxis in the eyes of newborn infants: a comparison of silver nitrate and erythromycin.** Missouri Med. **53**:187-190, March, 1956.

Conjunctival prophylaxis was alternated in a total of 12,599 infants born in five teaching hospitals in St. Louis. 5,489 infants received 1-percent silver nitrate solution and 7,110 infants erythromycin ophthalmic ointment. No case of gonorrheal ophthalmia was observed. Erythromycin greatly reduced the number and severity of conjunctival reactions. Erythromycin ophthalmic ointment was found to be easy to apply, stable without refrigeration, and equally or more effective than silver nitrate against gonococcal infection. (1 table, 11 references) Irwin E. Gaynon.

Weinstein, E. **A new method of studying the optic canals.** Vestnik oftal. **34**: 37-39, Sept.-Oct., 1955.

Weinstein modified the method of roentgenographic examination of the optic foramen of Rhese in that he puts the patient on his back instead of face down. This makes the examination of patients with extensive injuries of the face, or marked exophthalmos, and children of pre-school age possible. He also uses a narrower tube (than Rhese). This method is simple and can be used in most of the clinics. (5 figures) Olga Sitchevska.

6

OCULAR MOTILITY

Barthelmess, G. **Projection coordination with luminous targets for the examination of heterotropia.** Klin. Monatsbl. f. Augenh. **128**:186-195, 1956.

The angles of deviation are measured in various directions of gaze. The targets are projected on a screen and viewed with a red-green glass. A Hess screen is used for recording. The congruence test of Tschermak and the four-dot test of Worth can also be projected. (5 figures, 19 references) Frederick C. Blodi.

Focosi, M. and Guzzinati, G. C. **The head tilting test in the study of vertical components associated with horizontal strabismus.** Ophthalmologica **130**:283-294, Oct., 1955.

The authors found the head tilting test to be of value in deciding whether a vertical deviation in concomitant horizontal squint should be corrected surgically by recession of one inferior oblique muscle or resection of the contralateral superior rectus muscle. In 19 out of 24 such cases the head tilting test suggested overaction

of one inferior oblique muscle secondary to underaction of the ipsilateral superior oblique. In the remaining five cases the head tilting test spoke for underaction of one superior rectus muscle. The results of surgery based on the head tilting test were remarkably good.

In some cases of horizontal concomitant strabismus the head tilting test may be difficult to perform, because of 1. small amounts of vertical deviation, 2. marked amblyopia of one eye, making its recovery movement very indefinite, 3. very high degrees of horizontal deviation, and 4. underaction of several vertical muscles. In case 1. no correction of the vertical deviation is necessary. In case 2. definite measurements may be obtained with the help of large fixation objects. In case 3. it may be necessary first to reduce the horizontal deviation by surgical means. (2 figures, 21 references)

Peter C. Kronfeld.

Linksz, Arthur. **Ocular axes and meridians during oblique oculorotations.** A.M.A. Arch. Ophth. **55**:380-396, March, 1956.

For the limited excursions which the eye is actually able to make in oblique rotations, one may say that extorsion of both the corneal and the retinal diameters occurs when the eye turns upward and outward, or downward and inward, around an oblique axis situated in Listing's plane. Intorsion occurs in the other eventualities and the false torsion is always in the same direction. This confirms Dr. Pascal's last statement on the subject. (11 figures, 23 references)

G. S. Tyner.

Reusch, Ernst. **The treatment of heterotropia in adults.** Klin. Monatsbl. f. Augenh. **128**:199-102, 1956.

Thirteen adult patients with good binocular vision were treated by surgery and orthoptics. In 10 of them fusion developed. (1 table, 2 references)

Frederick C. Blodi.

Siebeck, Robert. **Binocular vision in congenital and early acquired disturbances of ocular motility.** Klin. Monatsbl. f. Augenh. **128**:173-181, 1956.

Seven patients are analysed. All of them had a paralytic strabismus since birth or since the first year of life. All of them had good binocular vision, even stereopsis. These findings speak against a primary motor disturbance as the etiology of concomitant strabismus. (1 figure, 73 references) Frederick C. Blodi.

Starkewicz, W. and Borodzicz, B. **Late results of squint surgery.** Klinika Oczna **25**:1-8, 1955.

The results of surgery in 508 cases of strabismus are reviewed. In convergent squint the cosmetic result was satisfactory (within 5°) in about 70 percent, uncorrected in 20 percent, and overcorrected in 10 percent. In divergent squint results were satisfactory in children in 50 percent and in adults in 60 percent. In cases where visual acuity of one eye was below normal the final results were worse than in cases with good visual acuity in both eyes. The amplitude of eye movements was affected very little by the operation. (5 figures) Sylvan Brandon.

7

CONJUNCTIVA, CORNEA, SCLERA

Alberth, B. **Autokeratoplasty. Covering of the defect with lyophilized human cornea.** Szemészet **4**:169-171, 1955.

A disc taken from the transparent cornea of the blind right eye was transplanted into the leukoma of the left eye. The defect of the right eye was replaced by a piece of human lyophilized cornea stored at room temperature for 152 days.

The latter graft adhered but became grey, while the autotransplant remained transparent. Vision is 0.1. Gyula Lugossy.

Cagianut, B. and Theiler, K. **Kayser-Fleischer's corneal ring (hepatolenticular degeneration).** Arch. f. Ophth. **157**:302-312, 1956.

Two cases of Struempell-Wilson's disease with Kayser-Fleischer rings were histologically and chemically studied. The pigment was found to be deposited in Descemet's membrane, not in the endothelium. Histochemical, spectrographic and chemical analyses made it most probable that silver is the essential material forming the corneal pigment ring. In addition to this finding the authors report that spectrographic studies demonstrated in the diseased corneas the presence of silver, copper, nickel, iron, calcium, aluminum, sodium and magnesium while normal corneas showed the presence of copper, calcium, aluminum, sodium and magnesium. (6 figures, 1 table, 19 references) Ernst Schmerl.

Hertzberg, R. **Megalocornea: report of a case.** M. J. Australia **1**:287-288, Feb. 18, 1956.

A case of megalocornea is reported briefly. The corneas measured 16 mm. in diameter. (1 figure, 1 reference) Ronald Lowe.

Nagy, F. and Imre, Gy. **Genesis and treatment of corneal ulcer due to pseudomonas pyocyanea.** Szemészet **1**:13-18, 1956.

The source of infection is occasionally the fluoresceine solution contaminated with pseudomonas pyocyanea. Therefore, it should be replaced by a 2-percent mercurochrome solution or properly treated and often changed. Some strains are sensitive to streptomycin. Infections with such strains heal after subconjunctival streptomycin injections. All strains are susceptible to terramycin. If this drug be given subconjunctivally at an early period, the ulcer will heal. Gyula Lugossy.

Oppel, O. **Tumorlike degeneration of the conjunctiva.** Klin. Monatsbl. f. Augenh. **128**:145-158, 1956.

An eight-year-old boy, who for six years had had chronic conjunctivitis, developed a massive thickening of the palpebral conjunctiva in both eyes. Biopsy showed a hyaline and amyloid degeneration of the conjunctiva. All bacteriologic tests remained negative, but an old trachoma was thought to be present (family history, patient was a refugee from Russia).

Serum globulins were elevated and this makes the author speculate that hyaline and amyloid, as degenerated proteins, are precipitated from the bloodstream and not produced locally. Steroids may be of therapeutic value. (6 figures, 1 table, 38 references) Frederick C. Blodi.

Simison, E. V. **Conjunctival myiasis with oestrus ovis larvae.** A.M.A. Arch. Ophth. **55**:417-418, March, 1956.

A case of conjunctival infestation of an eye with larvae of the sheep nasal botfly, Oestrus ovis, is described. (1 figure, 3 references) G. S. Tyner.

Sztrilich, L. **Trachoma and helminthiasis.** Szemészet **1**:40-44, 1956.

Ova of intestinal worms were looked for in 294 trachoma patients and 255 healthy persons. Out of the 544 examinations 195 were positive, 394 negative. In the trachoma group 50 percent harbored worm ova, in the healthy group only 18.4 percent did. Little difference was seen in the distribution of worms, trichuris trichuria predominating in both groups. Thus, no one kind of worms may be held responsible for the preservation of trachoma. Both, trachoma and helminthiasis, bear close relation to general hygiene, and it is

in this point that they are related to each other. The influence of environment and general hygiene on both conditions is emphasized. In cases of resistant or recurring trachoma of children, helminthiasis is always to be sought for.

Gyula Lugossy.

Ziobrowski, Szczesny. **Case of complicated mycosis of the cornea.** Klinika Oczna **25**:59-62, 1955.

Mycotic corneal ulcer in a man, 28 years of age, is described. It followed a minor injury to the left eye by a twig. Initially the lesion resembled ulcus serpens and only after four weeks of unsuccessful treatment did its appearance suggest mycotic infection. Local application of a 1-percent solution of iodine and later a 1-percent aqueous solution of mercurochrome was followed by healing but there was considerable scarring. (10 references) Sylvan Brandon.

8

UVEA, SYMPATHETIC DISEASE AQUEOUS

Calhoun, F. Phinizy, Jr. **Diseases of the uveal tract.** A.M.A. Arch. Ophth. **55**:419-438, March, 1956.

A review of the available papers on disease of the uveal tract for the period from October, 1954 to October, 1955. The review covers congenital defects, degenerative and circulatory conditions, inflammations, cysts and tumors, and miscellaneous entities. (170 references) G. S. Tyner.

9

GLAUCOMA AND OCULAR TENSION

Cristini, G. and Fiorini, G. **The origin and relationship of mydriasis and ocular hypertension in chronic primary glaucoma.** Ann. d'ocul. **188**:1025-1032, Nov., 1955.

The authors studied the changes in intraocular pressure and pupillary response to adrenaline, which follow novocaine block of various sympathetic fiber components to the eye. They conclude that the vasomotor fibers for the uvea and the dilator fibers for the iris run together, and that both pupillary dilatation and ocular hypertension in glaucoma result from active sympathetic impulses of extraocular origin. They suggest that the abnormal stimuli may have their origin in the adventitia of the ophthalmic and internal carotid arteries (3 tables; 9 references)

John C. Locke.

Fanta, H. **Histologic study of an eye with posterior surgical fistula.** Arch. f. Ophth. **157**:278-286, 1956.

In some types of glaucoma Lindner had tried to depress the tension by production of a fistula about 10 mm. behind the limbus on the temporal side and below. However, in 9 out of 151 eyes operated upon this led to retinal detachment. The author describes the histologic findings in an eye which had to be enucleated. Retinal rupture and detachment seemed to be caused by a shrinking of the tissue around the trephined area. Vitreal, preretinal and intraretinal hemorrhages were seen. The scleral fistula was closed by newly formed conjunctival connective tissue. (6 figures, 3 references)

Ernst Schmerl.

Lowenstein, Otto. **The diencephalon and primary glaucoma.** Ann. d'ocul. **188**: 981-1024, Nov., 1955.

In primary glaucoma, a characteristic pupillary syndrome is found by means of pupillography. This consists of: 1. irreversible "tonohaptic" shape of the pupillary reflex to light, with shortened period of latency and increased speed of contraction, 2. normal psychosensory dilatation and absence of psychosensory restitution (dissociation phenomenon), and 3. absence of the second phase of dilatation

of the reflex to darkness. Clinical experience indicates that this syndrome is due to damage in the diencephalon or its connections to the midbrain, interfering with inhibitory fibers to the nucleus of the third nerve.

The same pupillary syndrome can be experimentally produced in monkeys by severing the supranuclear inhibitory fibers to the sphincter nucleus. Electrical stimulation of the dorsal hypothalamus and ventral thalamus, in the cat, causes variations of intraocular pressure not associated with parallel changes in systemic blood pressure or other observed autonomic functions. The pathologic process giving rise to the pupillary syndrome of primary glaucoma must therefore be situated in this area or its connections with the midbrain.

The constant association of variations of pathologic pressure with a characteristic pattern of pupillary reflex in glaucoma must be explained by the assumption that these are due to a process involving neighboring centers or fiber connections. The disturbance of the central nervous system must be primary and the peripheral ocular lesions secondary. While the afferent and efferent pathways to and from these centers as well as the receptor and effector organs in the eye are unknown, it is unlikely that the cervical sympathetic or third nerve play a direct major role. The assumption that nervous factors affect the inflow-outflow system of the eye by neurovascular mechanisms exclusively does not take into account the fact that the nervous system regulates not only vascular activity, but also the state and function of all body tissues, including those structures in the eye under consideration by the "mechanical school." A number of neurogenic mechanisms are imaginable, including that of a direct or indirect influence of nervous centers on membrane permeability. (17 figures, 1 table, 23 references) John C. Locke.

Sedan, J., Jayle, G. E., Ourgaud, A. G. and Arnoux, M. **Results of 374 fistulizing operations observed for more than four years after surgery.** Ann. d'ocul. **188**:1039-1041, Nov., 1955.

While all cases in this series were followed for at least four years, 56 have been followed from 10 to 20 years, and 12 cases for over 20 years. Elliot trephine was employed in 263 cases, Lagrange sclerectomy in 109, iridencleisis in one, and iridectomy with self-fistulization in one. All but 62 patients have normal tension. Perimetric results are difficult to interpret, but generally speaking the fields were stabilized in favorable cases, and became progressively worse in unfavorable ones. In 40 patients (10.6 percent) an actual improvement in the visual field occurred postoperatively. Visual acuity results have given the most precise data. While not the chief way of evaluating chronic glaucoma, any patient operated on several years previously and maintaining the same visual acuity, can without gross error be considered stabilized. Where an operation was unsuccessful from tonometric and perimetric points of view, it was unusual for the vision to be conserved.

Results fall into three main groups: 1. in 23 cases, vision was less than 1/10 before operation, and either remained the same or decreased postoperatively, 2. in a favorable group of 203 cases, vision better than 1/10 was retained (average loss was minimal) and 3. in a group of 48 major failures, a preoperative vision of better than 1/10 dropped to less than 1/10 after surgery. Causes of failure were: obliteration of the fistula in 21 cases; nonoperable cataract or unsuccessful operation in 14 cases; progressive optic atrophy in spite of normal ocular tension in 10 cases; staphylomatous ectasia of the fistula in 3 cases; delayed acute panophthalmitis in one and delayed iridocyclitis in one case. The average vision in the last group before operation was significantly less than

that in the second indicating that better results will be obtained when surgery is carried out earlier in the course of the disease. The results also suggest an "all or nothing" effect from surgery, that is, the disease is either stabilized or the patient becomes blind. John C. Locke.

Viallefont and Boudet. **Sleep therapy in ophthalmology.** Ann. d'ocul. **188**:1033-1038, Nov., 1955.

The authors have been able to observe beneficial effects of sleep therapy in several cases of glaucoma. The treatment must be carried out in the early stages of the disease before irreversible organic changes have taken place. It is contraindicated in cardiac decompensation, renal and hepatic insufficiency, severe diabetes, in children and in the aged. Using combinations of barbiturates and largactil, sleep is induced for periods of 18 hours a day for a total of ten days. The patient is then allowed to return to his usual rhythm in gradual steps over a period of several days. If it is admitted that abnormal cortical excitation underlies those functional disorders which lead to organic disease, it can be understood how sleep therapy, by interrupting harmful conditioned reflexes, allows normalization of neuronal circuits and of impulses to the diseased organ.
John C. Locke.

10
CRYSTALLINE LENS

Sz. Bródy, M. and Henter, K. **Observations in 970 cataract operations performed with direct rupture of the zonula fibers.** Szemészet **1**:4-12, 1956.

By using the direct zonula rupturing method of Béla Horváth, intracapsular extraction was carried out in 88 percent of the cases of extreme myopia, in 93 percent of the complicated and in 66 percent of the pathologic cataracts. The procedure was of particular advantage when the capsule was swollen, thin, and fragile. Further, the method is promising in all other cases also in which intracapsular extraction is possible. In the authors' department, the ratio of intracapsular extractions is 83 percent in general, 93.4 percent for the most skilled operators.
Gyula Lugossy.

Ferguson, T. M., Rigdon, R. H. and Couch, J. R. **Cataracts in vitamin E deficiency.** A.M.A. Arch. Ophth. **55**:346-355, March, 1956.

The authors found that turkey embryos obtained from hens which were deficient in vitamin E show extensive liquefaction of the lens protein and focal areas of degeneration in the cornea and, in severe cases, degeneration of the epithelium of the lens. The latter will be present on the posterior surface of the lens. Sometimes turkeys permitted to hatch from these hens have bilateral cataract. (15 figures, 10 references) G. S. Tyner.

Haik, G. M. and Jimenez, T. **The mechanics of intracapsular cataract extraction: description of a technic for subluxation of the lens without trauma.** South. M. J. **49**:209-215, March, 1956.

The classical technique of Smith, Barraquer, Knapp, Török, Verhoeff and Kirby are briefly reviewed. Experiments on twelve enucleated eyes are described, wherein an attempt is made to find the optimum site and means for exerting pressure to subluxate the lens. It is suggested that the safest method is to apply pressure to the posterior lip of the wound with a lens loop at the 10, 12 and 2 o'clock positions aiding the subluxation of the lens by exerting counterpressure with a muscle hook below. The lens is then delivered by tumbling. (3 figures, 10 references)
Harry Horwich.

Lisch, Karl. **Congenital malformation of the lens.** Arch. f. Ophth. **157**:287-293, 1956.

A case of lenticonus posterior is reported and the literature on lenticonus posterior and microphakia is discussed. Abnormalities of the tunica vasculosa lentis are considered pathogenetic factors in both conditions. (3 figures, 19 references) Ernst Schmerl.

Lugossy, Gy. **Bilateral cataract operations.** Szemeszet **1**:30-32, 1956.

The cataract was removed from both eyes at the same time in 50 patients. Papolczy's suture was used in all the operations. In 42 patients intracapsular extraction with a round pupil was performed on both eyes. In these 100 eyes intracapsular extraction with intact capsule was achieved in 96 percent, extracapsular extraction in 2 percent, extraction with a partially opened capsule in 2 percent, and with a round pupil in 92 percent. Gyula Lugossy.

11

RETINA AND VITREOUS

Miratynska-Rusinowa, E. and Lisiecka-Adamska, H. **Diabetic retinopathy.** Klinika Oczna **25**:37-48, 1955.

The authors found diabetic retinopathy in 142 of 750 diabetics, or 19 percent, and mostly in subjects over 40 years of age. No relation between the duration of diabetes and the appearance of diabetic retinopathy was noted; however, the retinopathy appeared more frequently in severe diabetes. Retinopathy of the type associated with diabetes occurred in four patients who had chronic pancreatitis but no diabetes. The authors feel that the retinopathy may be caused by a disturbance in the pancreas and not strictly by the diabetes. It was more frequent in obese diabetics than in those of normal weight. There was no relation to hypertension, arteriosclerosis or renal changes. (7 tables, 35 references) Sylvan Brandon.

Yung-Lin, Hu. **Unilateral primary pigmentary degeneration of the retina.** Chinese M. J. **73**:524-526, Nov.-Dec., 1955.

A case (the seventeenth to be reported) of unilateral pigmentary degeneration of the retina in a 21-year-old man is reported. (6 references) Irwin E. Gaynon.

12

OPTIC NERVE AND CHIASM

Kurachi, Y. and Yonemura, D. **Critical fusion frequency in retrobulbar neuritis.** A.M.A. Arch. Ophth. **55**:371-379, March, 1956.

The authors describe the behavior of critical fusion frequency of flickering light (CFF) in patients with retrobulbar neuritis. Experiments were carried out with special reference to the CFF at the retinal region corresponding to the central scotoma.

As the area of the stimulating target was increased, the CFF in the patients failed to increase within the central area showing the scotoma. A similar result was obtained in studies of the effect of an increase in stimulus intensity upon the CFF. The similarity in congenital achromatopsia retrobulbar neuritis is noted. It is possible that the block in the nerve impulses in "retrobulbar" neuritis may be in the neuronal network in the bipolar cell, instead of in the nerve fibers behind the globe. (6 figures, 12 references) G. S. Tyner.

Senà, J. A., Cerboni, F. C. and Kutyn, J. **Hyaline bodies (Drusen) of the optic discs.** Arch. oftal. Buenos Aires **30**:447-452, Nov., 1955.

In addition to a review of the literature, two cases of colloid bodies of the optic nervehead are presented. In these, a mother and a son, the anomaly appeared as an isolated defect and was responsible for a marked narrowing of the field on the nasal side and, in one instance only,

for a much-impaired visual acuity. (3 figures, 13 references)

A. Urrets-Zavalia, Jr.

13

NEURO-OPHTHALMOLOGY

Lowenstein, Otto. **Miosis in Argyll Robertson syndrome and related pupillary disorders.** A.M.A. Arch. Ophth. **55**:356-370, March, 1956.

Pupillary diameter and reactions were recorded by pupillography of the dark-adapted eye. The characteristics of cases in the following categories are given: 1. miosis due to damage in the sympathetic pathways to the dilator muscle of the iris, 2. damage of the pathways of supranuclear inhibition which end in the Edinger-Westphal nucleus, and 3. miosis due to parasympathetic spasm. (12 figures, 2 tables, 7 references) G. S. Tyner.

Schmoeger, Elisabeth. **Myopia and von Recklinghausen's neurofibromatosis.** Arch. f. Ophth. **157**:260-277, 1956.

The author describes a family in which three girls show signs of a general neurofibromatosis and nodular lesions of the iris. The fourth child, a boy, is completely normal. One of the girls presents a neurinoma of the left upper lid, left-sided buphthalmus and enlargement of the orbit and of the optic channel. Another girl shows left-sided ptosis, myopia of about 10 D with amblyopia and divergent strabismus. An occasional correlation between high myopia and neurofibromatosis is considered similar to the one known between buphthalmus and Recklinghausen's disease. (6 figures, 61 references)

Ernst Schmerl.

15

EYELIDS, LACRIMAL APPARATUS

Baird, C. D. **Disease of the Meibomian glands.** Canad. M. A. J. **74**:437-440, March 15, 1956.

In this general review of disease of the Meibomian gland standard methods of diagnosis and treatment are set forth. The subjects covered are: chalazion, acute suppurative meibomianitis (hordeolum internum), chronic suppurative meibomianitis, chronic meibomianitis (seborrheic meibomianitis), acne (comedo), epithelioma arising from a Meibomian gland and its differential diagnosis, and infarcts of the Meibomian glands.

Harry Horwich.

Gáll, J. and Brooser, G. **Trachoma changes in the lacrimal pathways as reflected by the results of X-ray examinations.** Szemészet **1**:37-39, 1956.

In trachoma the permeability of the lacrimal ducts is not enough to exclude their affection. The points of attack are the physiologic narrow places, but early characteristic alterations may ensue in the wall of the lacrimal sac, and, later, in the canaliculus also. Of these, clear information cannot be obtained without a film taken after the injection of radiopaque substance. Gyula Lugossy.

Kwaskowski, Adam. **Plastic operation of the lid in the case of cancer of its margin.** Klinika Oczna **25**:9-14, 1955.

Malignant tumors of the lid margin should be removed surgically. The excision should be wide enough to prevent recurrence. The loss of tissue necessitates reconstruction of the lid. The author describes various methods of plastic procedure: Burow's, Elschnig's, Imre's and Kettesy's. The latter is favored by the author because of a better final cosmetic result. All of these procedures are based on a sliding flap of the skin. The difference is in the shape of the incision and formation of a "step" which gives later a well shaped lower lid. (11 figures, 9 references) Sylvan Brandon.

Lawson, Lawrence J. **Epiphora in infants.** J. Pediat. **48**:477-481, April, 1956.

The causes of epiphora are discussed etiologically, and then topographically as to puncta, canaliculi, lacrimal sac, nasolacrimal duct. The value of early intervention in cases requiring irrigation and probing is stressed; treatment before the age of three months is advised. (2 figures, 14 references) Harry Horwich.

Renfer, Hansrudolf. **Therapy of tumors of the skin of the medial canthus.** Strahlentherapie **99**:345-353, 1956.

On the basis of experience with 25 tumors the fractional small-distance irradiation with small, individual doses is recommended. One must be aware of the importance of conserving the function of the lacrimal duct. The cosmetic results were very favorable. (10 figures, 1 table, 24 references) Irwin E. Gaynon.

Starkiewicz, Witold. **Superior canaliculo-rhinostomy.** Klinika Oczna **25**:21-24, 1955.

The author analyzes the difficulties encountered in dacryocystorhinostomies. The main complication is the closure of the new opening into the nose and the loss of patency. A new method is suggested for use when the lacrimal sac is obliterated but both canaliculi are open and connected with each other. The superior canaliculus is dissected and passed into an opening through the bone; the superior end is sutured to the nasal mucosa. In five cases operation by this method resulted in good drainage and in one the lumen was obliterated. The patients were observed from one to three months. (3 figures, 7 references)

Sylvan Brandon.

Wolter, J. D., Stratford, T. and Harrell, E. R. **Cast-like fungus obstruction of the nasolacrimal duct.** A.M.A. Arch. Ophth. **55**:320-322, March, 1956.

A patient is described who had epiphora from obstruction of the nasolacrimal duct by a cast-like mass. Apparently the fungus C. albicans was the cause. (4 figures, 2 references) G. S. Tyner.

16

TUMORS

Bienengraeber, A. **Ophthalmic oncology from the viewpoint of general pathology.** Klin Monatsbl. f. Augenh. **128**:129-145, 1956.

This is a short review on the classification of tumors as they may affect the eye and the adnexa. (9 figures)

Frederick C. Blodi.

Herszenderfer, Alexander. **Malignant tumors of the eye and their treatment.** Klinika Oczna **25**:25-36, 1955.

Anatomic conditions of the eye and the orbit in their relation to the development of malignant tumors are described. For tumors of the lids surgical treatment is advocated and the importance of shielding the globe during X-ray treatment is emphasized. Melanoma requires considerably wider excision than carcinoma. Tissue with precancerous changes should be removed to avoid more extensive surgery later. Tumors on the surface of the globe are not frequent. Melanomas require exenteration of the orbit. Intraocular tumors require radical surgery; melanomas are seen in adults and retinoblastomas in children. The clinical course and diagnostic manifestations of intraocular tumor are presented. Metastatic tumors of the uvea are mentioned. (9 references)

Sylvan Brandon.

Nover, Arno. **Occurrence of multiple primary malignant tumors.** Arch. f. Ophth. **157**:237-259, 1956.

In a small number of cases the simultaneous occurrence of different types of primary malignant tumor in the eye and in other parts of the body is described. It seems to be the purpose of the study to

draw attention to the co-existence of multiple malignancies. (8 figures, 94 references) Ernst Schmerl.

17

INJURIES

Schmoeger, Elisabeth. **Electroretinography in siderosis and chalkosis.** Klin. Monatsbl. f. Augenh. **128**:158-166, 1956.

The first patient still had 6/6 vision in a siderotic eye and the ERG looked normal. The second patient had 0.6 vision in the injured eye and the ERG was evenly depressed. The third patient saw 0.9 and had a completely negative ERG.

In addition a comparative evaluation was done changing the light intensity. The corresponding response of the a and b wave can then be shown on a graph. Such an analysis gave abnormal curves even in the first patient who had a normal ERG with a high light intensity. In the second patient the b-wave was depressed and in the third one the a-wave.

The fourth patient had a chalkosis with a vision of 0.9. The ERG was practically normal. (9 figures, 2 references)

Frederick C. Blodi.

18

SYSTEMIC DISEASE AND PARASITES

Ainslie, D. and James, D. G. **Ocular sarcoidosis.** Brit. M. J. **1**:954-957, April 28, 1956.

The changes in the eye may suggest sarcoidosis but no eye signs are sufficiently characteristic to establish a diagnosis. Other clinical or radiologic data must be found to make the diagnosis tenable. Biopsy of skin lesions or enlarged superficial lymph nodes provide the most satisfactory support. In the absence of easily accessible lesions for biopsy the Kweim test is a simple, safe and specific method for providing histologic evidence of active sarcoidosis. It consists of the intradermal injection of an emulsion of sarcoid tissue in a saline solution. In patients with active sarcoidosis a dusky-red nodule develops at the site of injection in three or four weeks. When the test is positive histologic examination of the nodule reveals typical sarcoid tissue. (3 figures, 3 references) Irwin E. Gaynon.

Couran, O. F. and Waddy, B. B. **Effect of antrypol treatment of blindness due to onchocerciasis.** J. Trop. Med. **59**:52-56, March, 1956.

Antrypol given intravenously in doses of one gram weekly for five weeks can restore vision in many cases of blindness in which the lesion is due to onchocerciasis. Irwin E. Gaynon.

Hogan, Michael J. **Ocular toxoplasmosis.** A.M.A. Arch. Ophth. **55**:333-345, March, 1956.

Hogan reports on a conference of the Parasitology and Tropical Medicine Study Section of the National Institutes of Health. It was the collective opinion that it is not possible to make a diagnosis of toxoplasmosis on clinical ocular findings. The dye test is positive in a titer of 1:16 or more in 40 percent of patients of all types of uveitis, 50 to 60 percent in chorioretinitis, and 30 percent in iridocyclitis. (The latter is about the average for the normal population.) It was not possible to decide whether a negative dye test might rule out toxoplasmosis, except that in children under 10 a negative test can be considered as quite significant. The skin test alone is not sufficiently developed to establish the diagnosis of toxoplasmic uveitis, and the complement fixation test was felt to be of no value. Therapy with sulfadiazine alone and combined with pyrimethamine (Daraprim) showed markedly varying results in suspected cases.

The panel voted against recommending the establishment of a routine Public

Health Service for processing sera of patients with uveitis. (45 references)

G. S. Tyner.

Linton, R. G. and Saint, E. G. **The triple syndrome of Behcet; report of a case.** M. J. Australia **1**:502-504, March 24, 1956.

The authors describe in detail a woman, 34 years of age, who had recurrent stomal and vulvo-vaginal ulcers, severe arthropathy, recurrent pyrexia, urticaria, frequency of micturition, and three attacks of iridocyclitis. The symptoms were of seven years' duration and have been suppressed by the oral use of cortisone. (9 references) Hugh Ryan.

Szaloczi, K. **Ophthalmologic syndromes related to diseases of the organs of motion.** Szemeszet **4**:184-187, 1955.

The syndromes considered are those of Sjoegren, Reiter, Still-Chauffard-Felty, Rhonheimer, and scleromalacia perforans. According to the observations of the author, inflammatory eye diseases such as iridocyclitis and scleritis are, as a rule, associated with those diseases of the organs of locomotion in which inflammatory symptoms prevail, and the degenerative processes are secondary and of lesser significance. In contradistinction to this, degenerative eye processes, such as keratoconjunctivitis sicca and scleromalacia perforans occur in patients with primary chronic polyarthritis.

Gyula Lugossy.

19

CONGENITAL DEFORMITIES, HEREDITY

Gross, H. **Pathogenesis of optic atrophy in turricephalic dysostoses of the skull.** Arch. f. Ophth. **157**:225-236, 1956.

The autopsies of five children, three months to five years old, led to the assumption that the main cause of their optic atrophy was due to an error in development of the bony centers of the skull and absence of the coronary suture. The normal distension of the brain is interfered with, and by increased curving of its hemispheres the brain strives for the needed space. The brain stem is pulled upward and so are the optic tracts. This leads to their distension. Sooner or later an optic atrophy occurs, sometimes aggravated by nutritional disturbances due to venous congestion. (3 figures, 9 references) Ernst Schmerl.

Knoll, Á. **Simultaneous occurrence of pigment degeneration of the retina, and keratoconus.** Ezemészet **4**:165-168, 1955.

In a man, aged 27 years, pigment degeneration of the retina is associated with keratoconus. The association of the two morbid patterns is presumably, in the light of statistical data, not mere chance, but the result of close pathogenetic correlations. The coexisting glaucoma symptoms point to the functional disorders of the pituitary and the vegetative centers of the diencephalon. Gyula Lugossy.

20

HYGIENE, SOCIOLOGY, EDUCATION, AND HISTORY

Orlowski, Witold J. **Polish ophthalmic bibliography.** Klinika Oczna **25**:63-64, 1955.

The author lists 38 titles in the Polish ophthalmologic literature published in 1953 other than Klinika Oczna.

Sylvan Brandon.

Snyder, Charles. **A bibliography of the history of ophthalmology.** A.M.A. Arch. Ophth. **55**:397-407, March, 1956.

This paper is a compilation of the bibliography of the articles on the history of ophthalmology for the years 1952 through 1954. G. S. Tyner.

NEWS ITEMS

Edited by DONALD J. LYLE, M.D.
411 Oak Street, Cincinnati 19, Ohio

News items should reach the editor by the 12th of the month. For adequate publicity, notice of postgraduate courses and meetings should be received three months in advance.

DEATHS

Dr. Ralph Harrison Hopkins, Boston, Massachusetts, died February 29, 1956, aged 64 years.

Dr. Robert Scott Lamb, Washington, D.C., died March 4, 1956, aged 79 years.

Dr. Jacob Leonard Seidenstein, Saranac Lake, New York, died February 27, 1956, aged 55 years.

ANNOUNCEMENTS

PAN-PACIFIC SURGICAL ASSOCIATION

The seventh congress of the Pan-Pacific Surgical Association will be held in Honolulu, Hawaii, November 14 to 22, 1957. All members of the profession are cordially invited to attend and are urged to make arrangements as soon as possible if they wish to be assured of adequate facilities.

An outstanding scientific program by leading surgeons with sessions in all divisions of surgery and related fields promises to be of interest to all doctors.

Further information and brochures may be obtained by writing to

Dr. F. J. Pinkerton
Director General of the Pan-Pacific Surgical Association
Room 230, Young Building
Honolulu, Hawaii

VI ARGENTINE CONGRESS

The VI Argentine Congress of Ophthalmology will be held in the city of Mar del Plata, Argentine Republic, from April 9 to 14, 1957. The official subjects are "Cornea" (progress since 1935) and "Vertical strabismus." The speakers on these subjects will be:

Dr. A. Ferrer Arata, "Morphology of the cornea: Anatomy and histology"; Dr. Julio Arouh, "Semiology of the cornea"; Dr. Dante Dolzani, "Physiopathology of the cornea"; Dr. Carlos Laje Weskamp, "Pathologic anatomy of the cornea"; Dr. Virgilio Victoria, "Pathology of the cornea"; Dr. Alejandro Salleras, "Clinical treatment of the corneal diseases"; Dr. Pedro F. García Nocito, "Surgical treatment of the cornea"; Dr. Alberto C. Cremona, "Hereditary diseases of the cornea"; Dr. Jorge C. Zambrano, "Legal and social medicine in corneal affections."

Dr. Francisco Bellouard Ezcurra, "Etiology, pathogenesis and diagnosis of vertical strabismus"; Dr. Alberto Urretz Zavalía, "Treatment of vertical strabismus."

Further information may be obtained from:

Dr. Jorge Balza
Secretary of VIth Argentine Congress of Ophthalmology
P.O. No. 2699
Buenos Aires, Argentina.

MISCELLANEOUS

TV CATARACT SURGERY

Dr. Harold G. Scheie, secretary of the Section on Ophthalmology of the A.M.A. and professor of ophthalmology at the University of Pennsylvania, demonstrated the latest surgical technique in the removal of a cataract during the third and final program in the spring "March of Medicine" television series. The program, "Progress report —1956," originated from the A.M.A. annual meeting in Chicago and was picked up live from the University of Pennsylvania Hospital. The series was produced and sponsored by Smith, Kline & French in co-operation with the American Medical Association.

PERSONAL

Dr. Carroll R. Mullen, has been appointed professor and head of the Department of Ophthalmology at The Jefferson Medical College of Philadelphia.

NEW ORLEANS ACADEMY OF OPHTHALMOLOGY

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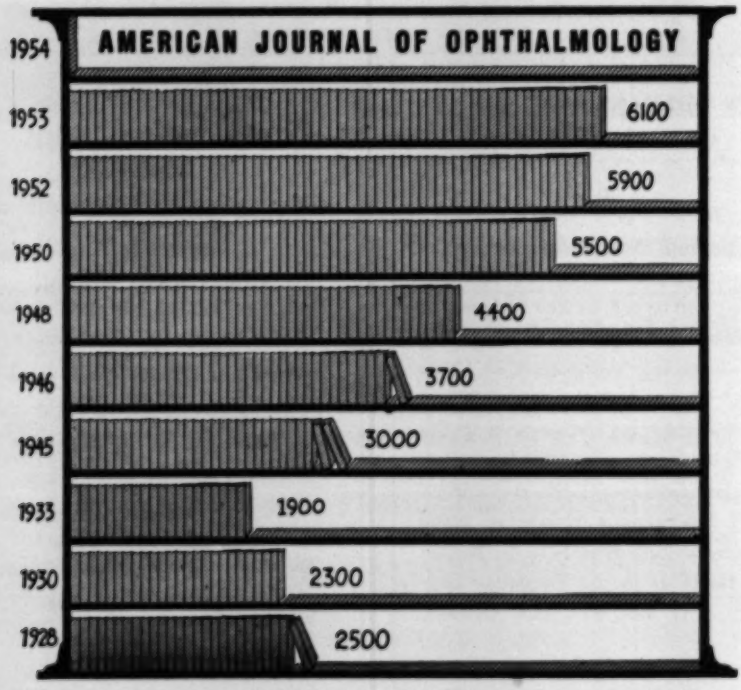
The Seventh Annual meeting of the New Orleans Academy of Ophthalmology will be held in New Orleans, in the Roosevelt Hotel—February 11-15, 1957, featuring "Symposium on Glaucoma." The registration fee of $75.00 includes associate membership in the Academy for the year 1957, as well as all other features of the convention. Hotel reservations should be made early by writing directly to the Roosevelt Hotel or to the Executive Secretary, P.O. Box 469, New Orleans, La.



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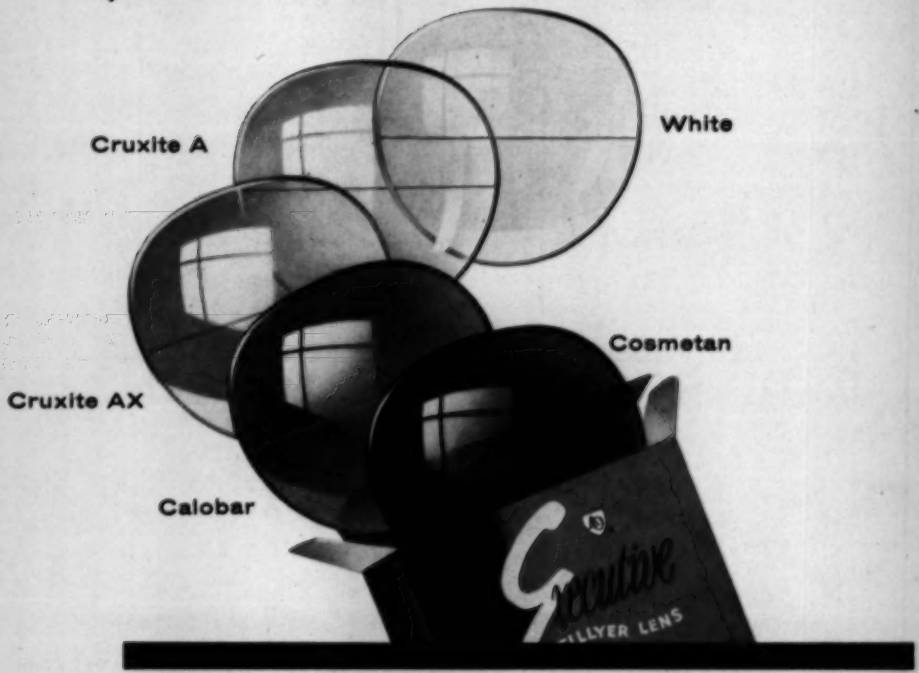

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